REGIONAL COMMUNITY WORKSHOP

Welcome and Announcements

Kelly Cox

IMF Senior Director, Regional Community Workshops

REGIONAL COMMUNITY WORKSHOP

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REGIONAL COMMUNITY WORKSHOP

REGIONAL COMMUNITY WORKSHOP

VIRTUAL REGIONAL COMMUNITY WORKSHOP

Saturday, November 14, 2020 | 10:00 AM-12:30 PM MT

INTERNATIONAL MYELOMA FOUNDATION

with support from:
Amgen, Bristol Myers Squibb, Janssen,
Karyopharm Therapeutics, and Takeda Oncology

Joseph Mikhael, MD

Chief Medical Officer – IMF

Nina Shah, MD

Professor, Department of Medicine

University of California, San Francisco (UCSF)

Kimberly Noonan, RN, ANP, AOCN

Dana-Farber Cancer Institute

IMF Nurse Leadership Board

REGIONAL COMMUNITY WORKSHOP

Southern USA Virtual Regional Community Workshop (RCW)

Times listed are in Mountain Daylight Time (MDT)

10:00 - 10:10	Welcome and Announcements from Kelly Cox
10:10 - 10:20	"Disparities in Myeloma"
	Joseph Mikhael, MD - TGen, City of Hope Cancer Center
10:20 - 10:40	"Myeloma 101 and Frontline Therapy"
	Joseph Mikhael, MD - TGen, City of Hope Cancer Center
10:40 - 10:55	Question and Answer Session with Panel
10:55 - 11:00	Stretch

REGIONAL COMMUNITY WORKSHOP

Southern USA Virtual Regional Community Workshop (RCW)

Times listed are in Mountain Daylight Time (MDT)

11:00 - 11:20 Relapsed Therapy and Emerging Therapies

Nina Shah, MD – University of California, San Francisco (UCSF)

11:20 - 11:35 Question and Answer Session with Panel

11:35 - 11:55 "Navigating the Journey"

Kimberly Noonan, RN, ANP, AOCN – Dana-Farber Cancer Institute

11:55 - 12:00 Closing Comments

Kelly Cox and Joseph Mikhael, MD

REGIONAL COMMUNITY WORKSHOP

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“Disparities in Myeloma”

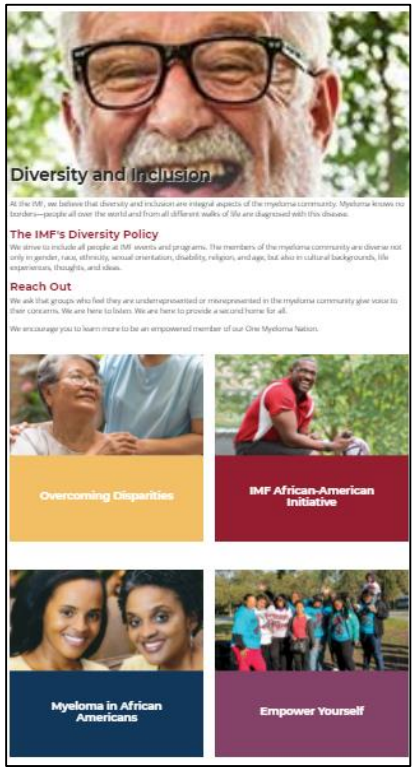
Joseph Mikhael, MD

TGen, City of Hope Cancer Center

REGIONAL COMMUNITY WORKSHOP

IMF Diversity Initiatives

Building on the IMF's Diverse History



Joseph Mikhael, MD, MEd, FRCPC
Chief Medical Officer, International Myeloma Foundation
Professor, Translational Genomics Research Institute (TGen)
City of Hope Cancer Center

What is Equity, Diversity and Inclusion?

- **Equity** means to guarantee of fair treatment, access, opportunity, and advancement for all while striving to identify and eliminate barriers that have prevented the full participation of some groups.

- **Valuing diversity** means that we recognize and respect everyone's unique qualities and attributes.

- **Inclusion** means that all individuals feel respected, accepted and valued.

INTERNATIONAL MYELOMA FOUNDATION

The IMF has had a history of supporting Diversity

The IMF has been deeply committed to ALL myeloma patients, worldwide…

The Global Myeloma Action Network (GMAN)

Support Groups

Activities in the African American, Hispanic and Asian communities (and more!)

Specific programs to help other vulnerable and disadvantaged individuals

Check out our website: https://www.myeloma.org/diversity/diversity-inclusion

INTERNATIONAL MYELOMA FOUNDATION

The IMF's Commitment to Diversity

We have created a "**Diversity Inclusion Team**"

This will oversee all aspects of diversity at the IMF

It will also serve as the core group to lead specific diversity initiatives at the IMF

eg. The African American Initiative

As with other IMF programs, it will include engagement, education, support and research

More details to follow!

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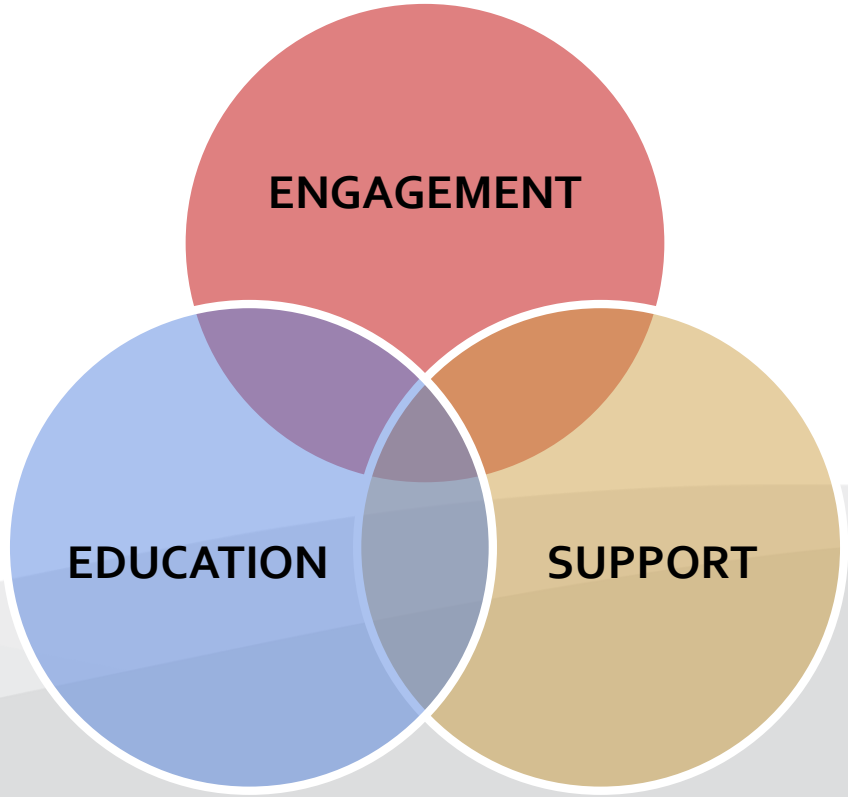
African American Initiative

The IMF African American Initiative is one important portion of the IMF's commitment to diversity and the wellbeing of all myeloma patients worldwide.

Many groups have sought to reach out to the African American myeloma community

HOWEVER

The IMF is ideally poised to make a difference due to its unique mission and presence in the community



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Important Facts about Myeloma and African Americans

1. Myeloma is the most common hematologic cancer in African Americans

2. MGUS and Myeloma is TWICE as common in African Americans

3. Survival improvements in myeloma have not been as pronounced in African Americans (For every 1.3 years of life gained for Whites, only 0.8 years of life gained for African Americans)

4. African Americans are younger at diagnosis by about 5 years

5. There is a longer time to diagnosis from the onset of symptoms

INTERNATIONAL MYELOMA FOUNDATION

Important Facts about Myeloma and African Americans

6. Africans Americans are less likely to receive TRIPLET therapies

7. African Americans are less likely to receive Stem Cell Transplants

8. Although African Americans comprise 20% of all MM patients, they only represent 5-6% of patients on clinical trials

9. There are biologic differences in African Americans with MM that may lead to lower risk disease

10. When African Americans receive equal access care, their survival outcomes are equal, and at times, better than Whites

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The IMF African American Initiative

The core vision of the IMF African American Initiative is to *improve the short and long-term outcomes* of African American patients through engagement of the community, education of health care providers, and support of patients

The overall objective of the IMF African American initiative is to improve outcomes in African American patient care by:

actively engaging the African American community in a better understanding of myeloma,

educating the primary health care community regarding early and accurate diagnosis of myeloma and

supporting the Hematology Oncology community in their care of African American patients with myeloma

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The Nursing Approach – IMF NLB

Build Trust

Engage the Community

Multiethnic Team

Cultural Competence

NURSE LEADERSHIP BOARD
A Division of International Myeloma Foundation

African American Patients With Multiple Myeloma

Optimizing care to decrease racial disparities

Amy Pierre, RN, MSN, ANP-BC, and Tiffany H. Williams, DNP, APRN, CPNP-PC

FIGURE 1.
CARE OF AFRICAN AMERICAN PATIENTS WITH MULTIPLE MYELOMA: NURSING BEST PRACTICES

ACCESS TO CENTERS OF EXCELLENCE

- Superior outcomes are noted for patients with multiple myeloma who are treated by multiple myeloma specialists, by oncologists with a high volume of patients with multiple myeloma, or at cancer centers of excellence. Nurses are encouraged to assist in decreasing the barriers to access to centers of excellence by engaging supportive resources for African American patients with multiple myeloma (i.e., social work and transportation assistance through foundations or grants).

OBTAINING A STEM CELL TRANSPLANTATION

- Recognition of stem cell transplantation eligibility at diagnosis and facilitating referral for a transplantation in a timely fashion should be incorporated in nursing care for African American patients with multiple myeloma.

ADHERENCE TO THERAPEUTICS/ SUPPORTIVE CARE

- Consistency with therapeutics improves outcomes for patients with multiple myeloma. Educating patients on this importance of adherence and assisting with the creation of treatment calendars, reminder apps for smartphones, and check-ins with patients can encourage adherence to improve outcomes.
- Creating patient literature prompting African American patients with cancer to ask questions about their diagnosis, treatment, side effects, daily life, coping strategies, and assistance with cost increases active participation in their oncology care.
- Having African American cancer survivors create video programs of their personal journey with cancer care or in- person, peer, one- on- one sessions discussing chemotherapy/ treatment for African American patients can improve adherence to follow- up cancer care and adherence to chemotherapy.

PARTICIPATION IN CLINICAL TRIALS

- Nurses should provide counsel to African American patients with multiple myeloma regarding the value of trial participation and actively engaging in seeking availability and eligibility of clinical trials. Actionable items include:
  - ☐ Early community engagement
  - ☐ Engaging patient advocacy groups to build trust
  - ☐ Cultural competency training for staff
- Community- based, culturally relevant cancer clinical trial education by way of modules, videos, and workshops has the potential to improve the ability of African American patients with cancer to make informed decisions about clinical trial selection and can also increase favorable attitudes about participation.

COMPETENCY IN UNIQUE CHARACTERISTICS OF DISEASE PRESENTATION/MANIFESTATION

Examples include earlier age at presentation, increased anemia, renal disease, comorbidities, obesity, lower- risk cytogenetics, and lower paraprotein levels with multi- organ involvement.

- Nurses must recognize the unique aspect that African American patients with multiple myeloma present at a younger age, have lower- risk cytogenetics, and lower monoclonal protein burden but higher comorbidities and multiorgan involvement. Nurses should anticipate disease- related complications for African American patients with multiple myeloma and encourage routine health maintenance and a healthy weight to improve comorbidities to maximize overall survival. Home- based, individually tailored physical activity interventions have sustained participation for African Americans.

CULTURAL DIFFERENCES

- Distrust of the medical profession can be an underlying issue in the care of minority patients due to the history of unethical medical treatment of African Americans in the United States. Building trust, perfecting cultural competence, and providing empathy are important for oncology nurses to achieve when caring for African American patients with multiple myeloma.
- Recommended cultural competency strategies include the following:
  - ☐ Show respect for cultural diversity.
  - ☐ Display a willingness to learn from patients.
  - ☐ Have an ethnically diverse healthcare team.
  - ☐ Appreciate/respect the role of the family in decision making.
  - ☐ Invest in and gain family trust.
  - ☐ Acknowledge/respect the role religion plays in decision making; participation in health activities can be influenced by church/religious leaders and can also be a foundation for information.
  - ☐ Avoid stereotyping and generalizations.
  - ☐ Build rapport and trust.
  - ☐ Address according to cultural preference.

Note. Based on information from Augustin et al., 2019; Banda et al., 2012; Blakeney et al., 2014; Brown et al., 2016; Eggly et al., 2017; Green et al., 2015; Hayney- Maslow et al., 2014; Pekmezi et al., 2018; Pérez et al., 2015.

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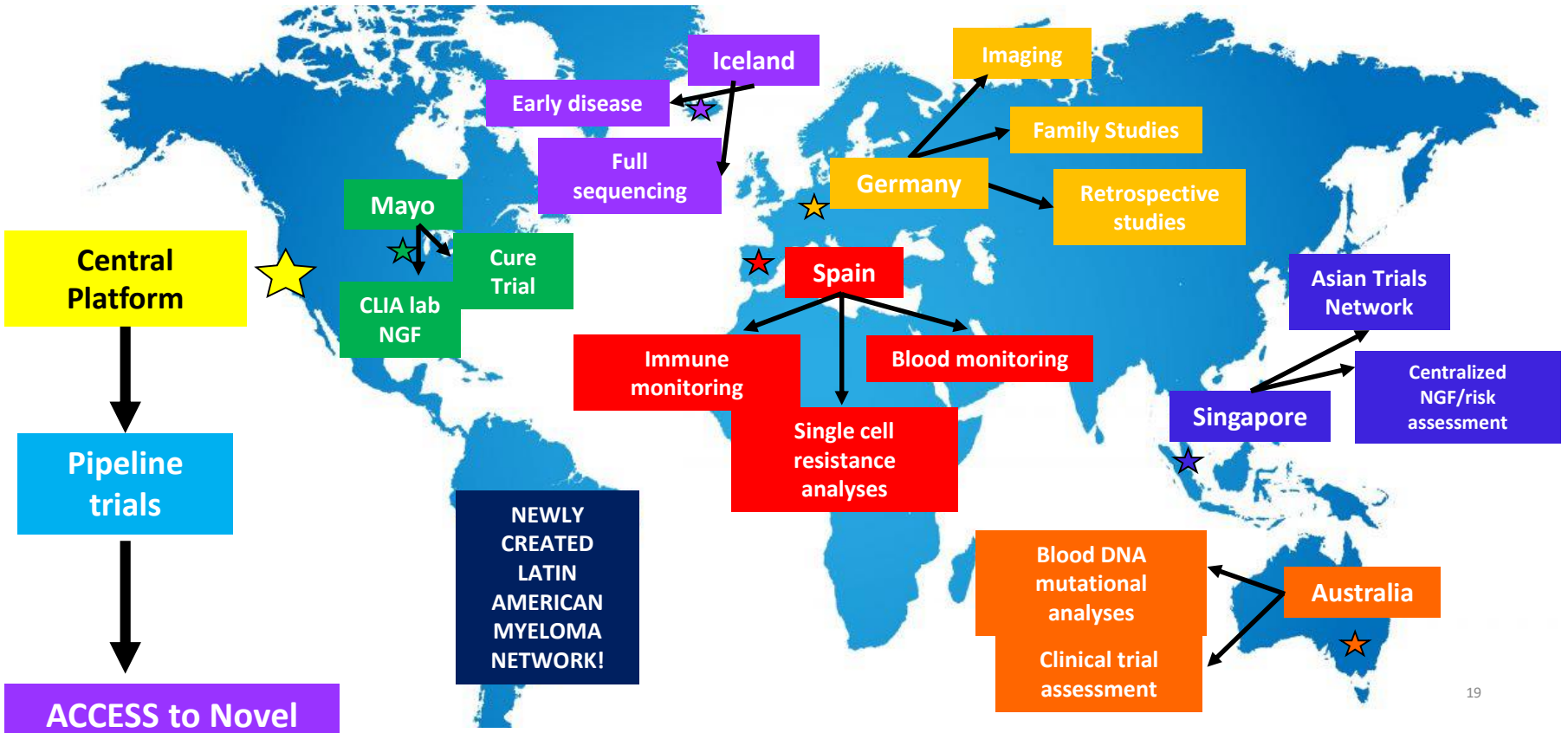
IMF Global Presence

Primary Goal is to cure Myeloma



Patients
Providers
Countries
Industry
Myeloma Community

THANK YOU!

Joseph Mikhael, MD, MEd, FRCPC

Professor, Translational Genomics Research Institute (TGen)
City of Hope Cancer Center

Chief Medical Officer, International Myeloma Foundation

Director of Myeloma Research and Consultant Hematologist, HonorHealth Research Institute

jmikhael@myeloma.org

INTERNATIONAL MYELOMA FOUNDATION

“Myeloma 101”
“Frontline Therapy”

Joseph Mikhael, MD
TGen, City of Hope
Cancer Center

REGIONAL
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Multiple Myeloma 101 and Frontline Therapy

IMF Regional Community Workshop

November 2020

Joseph Mikhael, MD, MEd, FRCPC
Chief Medical Officer, International Myeloma Foundation
Professor, Translational Genomics Research Institute (TGen)
City of Hope Cancer Center

Objectives

- Review the basics of blood and cancer
- Define multiple myeloma and its key features
- Highlight the approach to initial therapy for myeloma

The Basics of Blood

- The blood is an “organ” made up of both cells and liquid “plasma”
- Think of wine (red/white/rose)

1. Red Cells – carry Oxygen…trucks
2. White Cells – immune system…army
3. Platelets – help with clotting…ambulance

All produced in the blood factory = Bone Marrow

What is Cancer?

- Simple definition:
  - Identical, uncontrolled growth

- The body usually has a balance to allow cells to grow in the right place for the right period of time
  - When that system is unbalanced, cancers grow
  - Ie, solid tissue (breast, colon…) or blood cells

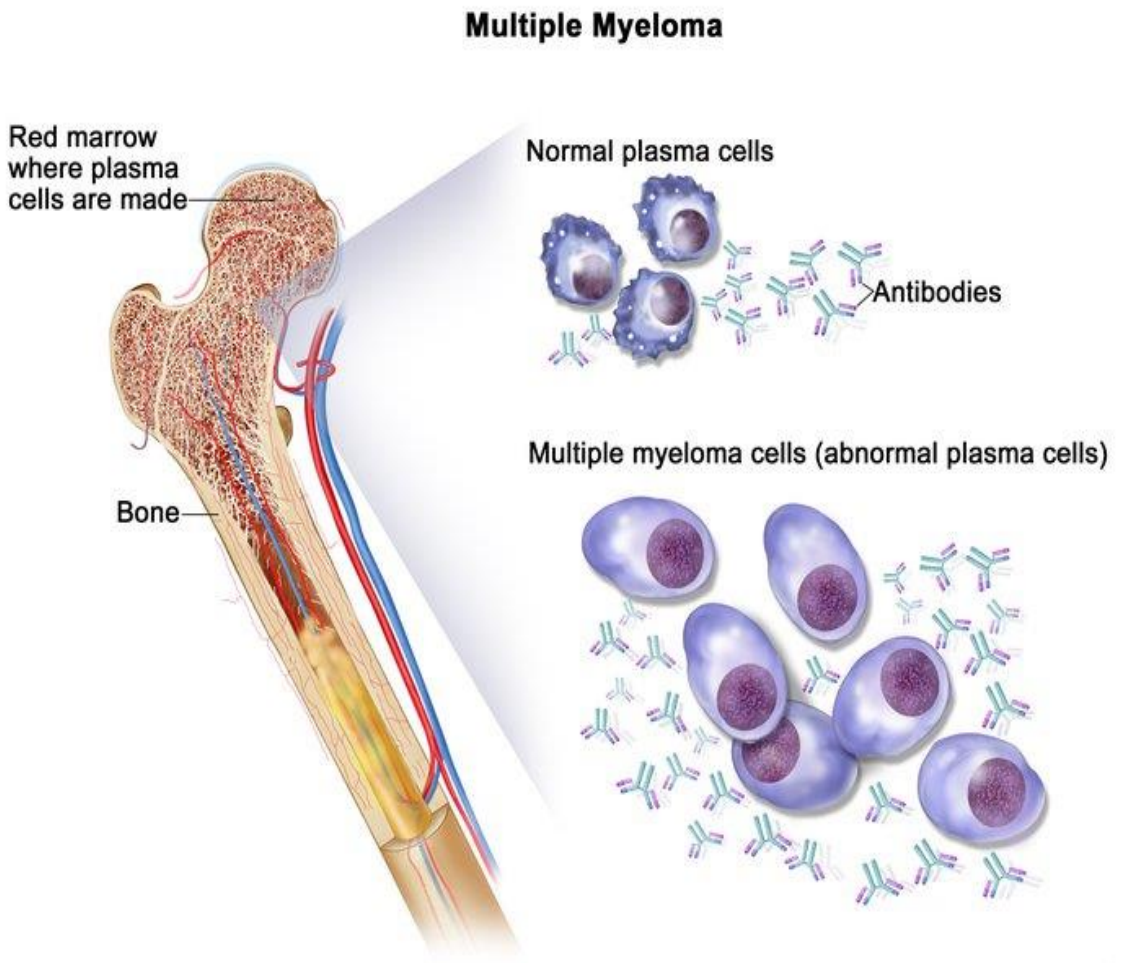
- The “double whammy” of blood cancers is that they are the cells meant to protect you
    - *citizen crime vs police crime*

What is Multiple Myeloma?

Multiple Myeloma* is a blood cancer that starts in plasma cells of the spongy center of bones (bone marrow).

- This is where stem cells mature into red blood cells, white blood cells, and platelets.
- Myeloma cells are abnormal plasma cells that make an abnormal antibody called “M protein”.

** Myeloma is **NOT** a bone cancer or skin cancer (melanoma), it is a type of blood cancer.*



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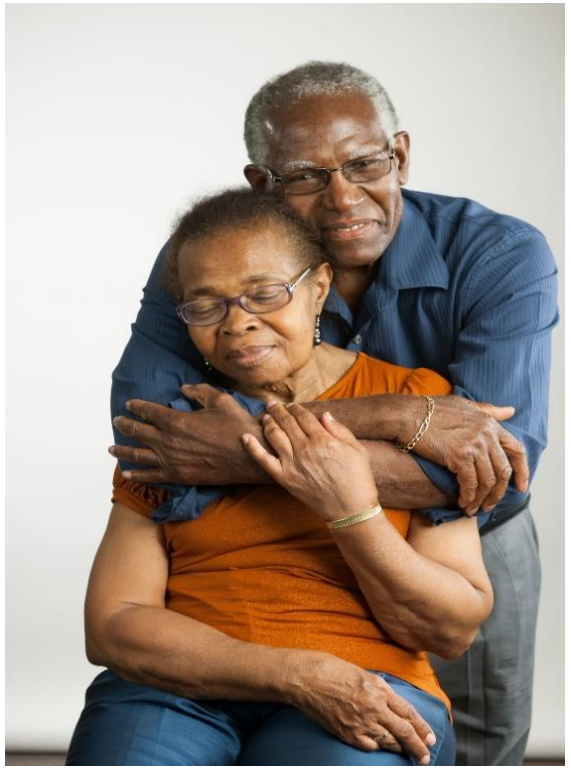
Who's at Risk for Multiple Myeloma

About 1 in 132 people are diagnosed each year
(MM is the second most common blood cancer diagnosed)



Your risk of myeloma increases if you are:

- Older than age 60
- African American (with a 2x greater risk than whites)
- Closely related to someone with MM
- A man (diagnosed more than women)
- Very overweight or obese
- Diagnosed with other plasma cell diseases, like MGUS (monoclonal gammopathy of undetermined significance).

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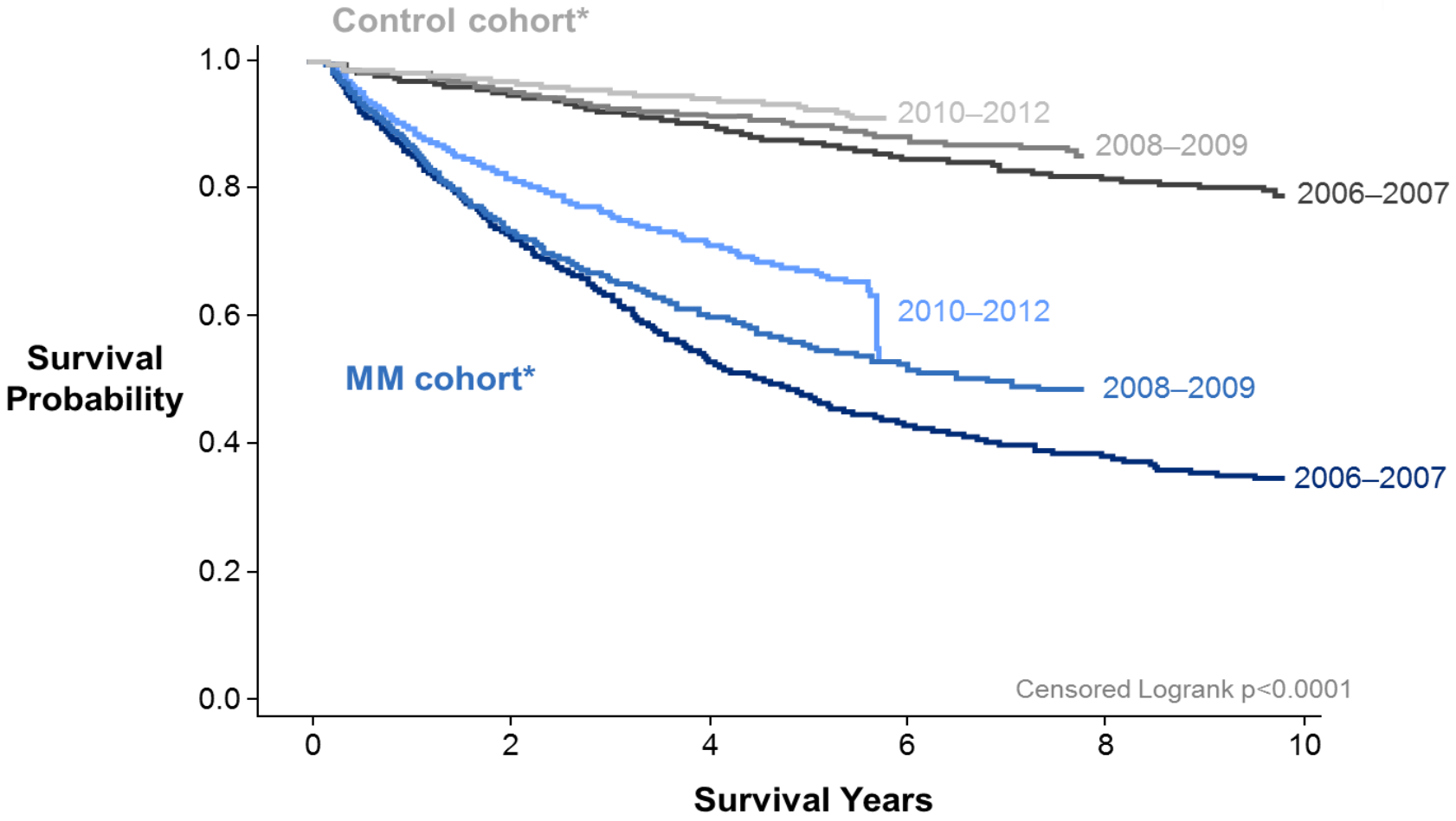
Improving Survival in MM



*Year ranges represent the year of diagnosis.
Note: By linking to the SSA Master Death File, survival was measured as time from diagnosis date to the date of death obtained from the SSA, time from diagnosis date to the date of inpatient death, or time from diagnosis date to September 30, 2015; Survival estimates were presented for multiple myeloma patients diagnosed and treated during 2006-2012 (n=9,521).

Fonseca B et al. Leukemia 2017;31:1915-1921.

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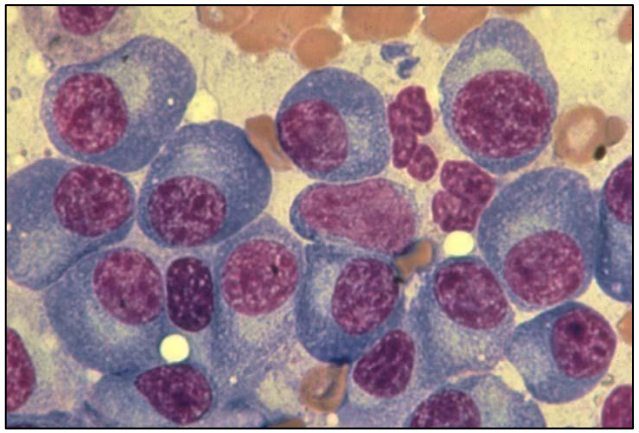
Myeloma Is a Cancer of Plasma Cells

- Cancer of plasma cells
- Healthy plasma cells produce immunoglobulins G, A, M, D, and E
- Myeloma cells produce abnormal immunoglobulin “paraprotein” or monoclonal protein



Bone marrow of patient with multiple myeloma

Image courtesy of American Society of Hematology
Kyle et al. *Mayo Clin Proc.* 2003;78:21-33;

FAST STATS

1.8% of all cancers;
17% of hematologic malignancies
in the United States

Most frequently diagnosed in ages
65 to 74 years
(median, 69 years)

In 2020:
32,000 estimated new cases;
13,000 estimated deaths

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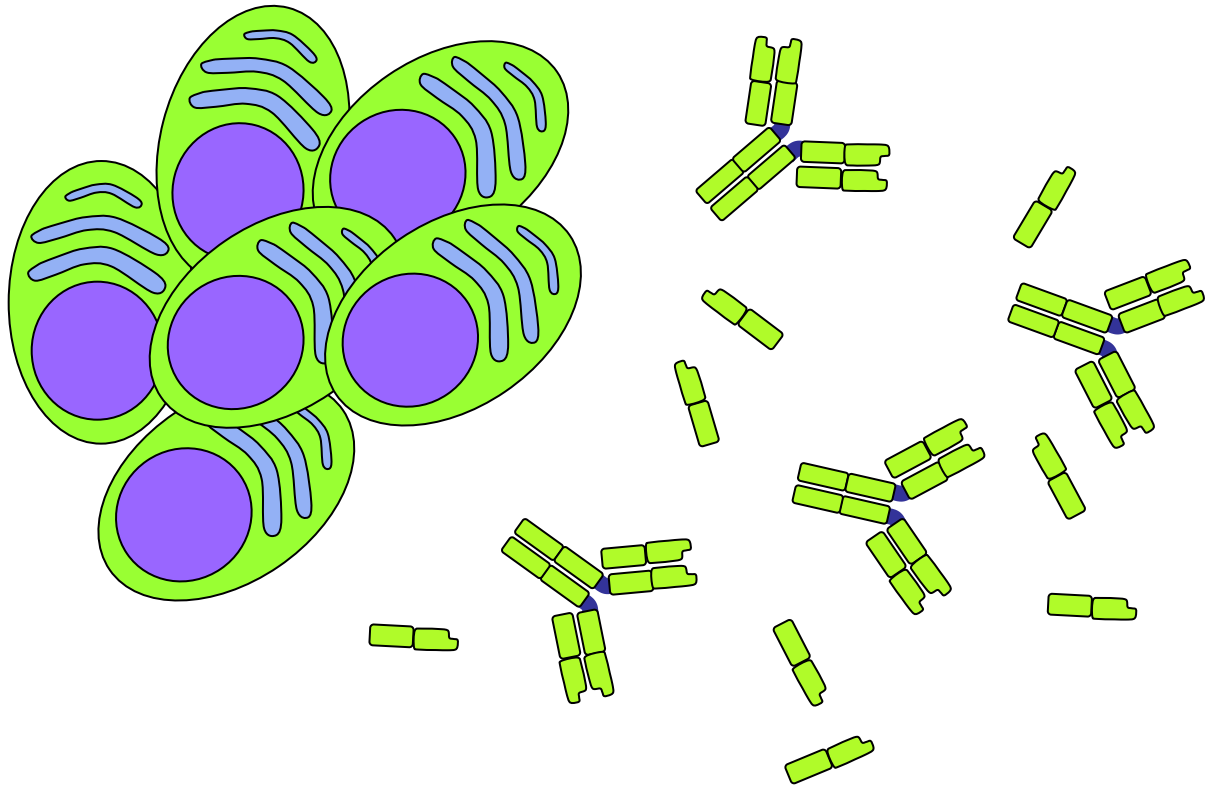
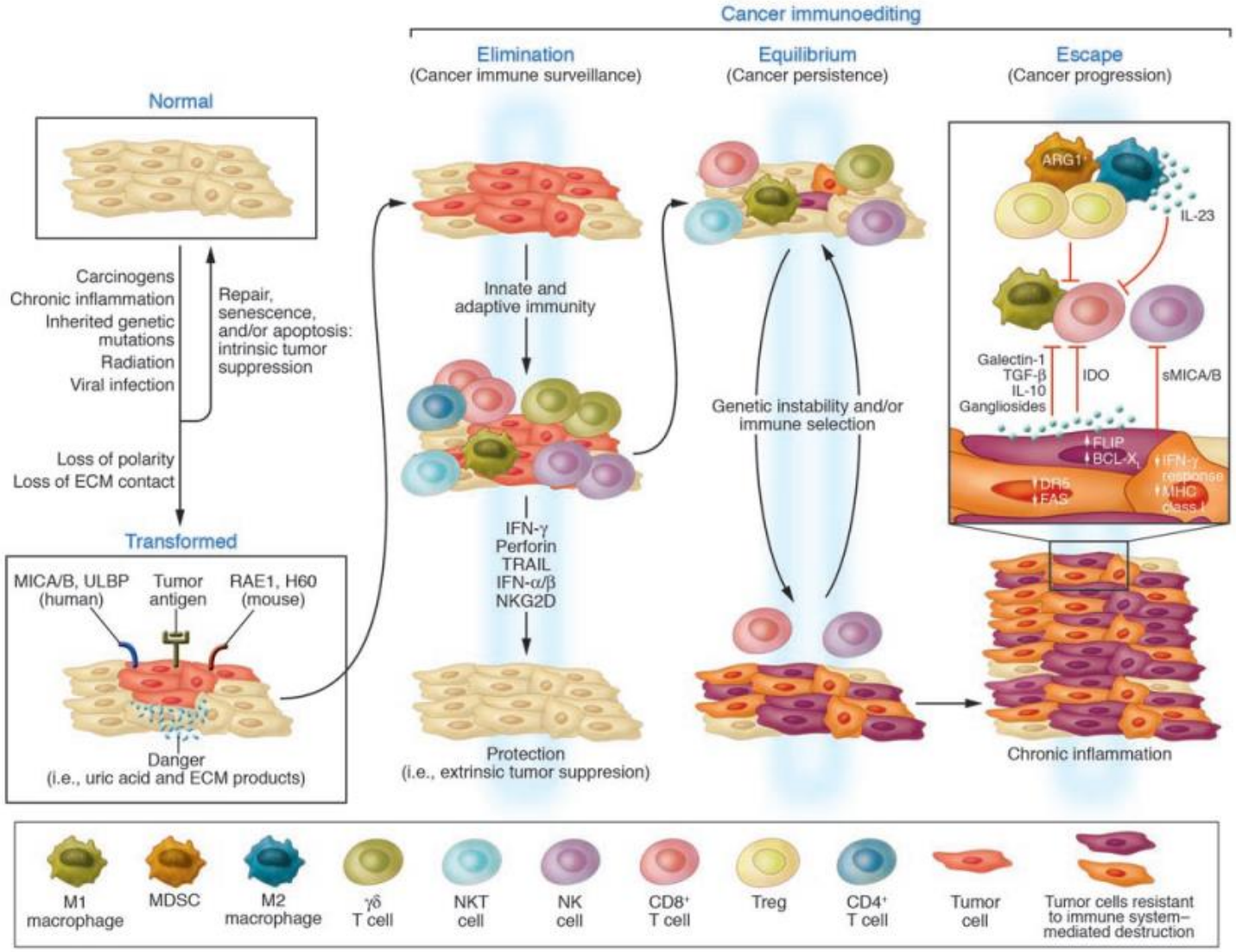
Diagnosis of multiple myeloma: Monoclonal immunoglobulin



The Immune System and Cancer – Myeloma is Classic



Swann JB & Smyth MJ. J Clin Invest. 2007 May 1; 117(5): 1137–1146.

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Multiple Myeloma Typically Preceded by Premalignant Conditions

	Premalignant		Malignant
Condition	**MGUS[1-4] (Monoclonal Gammopathy of Undetermined Significance)**	**SMM[1-5,8] (Smoldering Multiple Myeloma)**	**Active Multiple Myeloma[6-8]**
Clonal plasma cells in bone marrow	<10%	10%-60%	≥10%
Presence of Myeloma Defining Events	None	None	Yes
Likelihood of progression	~1% per year	~10% per year	Not Applicable
Treatment	No; observation	Yes for high risk*; No for others	Yes

* In clinical trial (preferred) or offer treatment for those likely to progress within 2 years

1. Kyle RA, et al. *N Engl J Med.* 2007;356:2582-90.
2. International Myeloma Working Group. *Br J Haematol.* 2003;121:749-57.
3. Jagannath S, et al. *Clin Lymphoma Myeloma Leuk*. 2010;10(1):28-43.
4. Kyle RA, et al. *Curr Hematol Malig Rep*. 2010;5(2):62-69.
5. Mateos M-V, et al. *Blood.* 2009;114:Abstract 614.
6. Durie BG, Salmon SE. *Cancer*. 1975;36:842-854.
7. Durie BG, et al. *Leukemia*. 2006;20(9):1467-1473.
8. Rajkumar SV, et al. Lancet *Oncology* 2014; 15:e538-e548.

2014 IMWG Active Myeloma Criteria: Myeloma-Defining Events

Clonal bone marrow ≥10% or bony/extramedullary plasmacytoma

AND any one or more **M**yeloma-**D**efining **E**vents

- **C**alcium elevation
- **R**enal complications
- **A**nemia
- **B**one disease

BM	Clonal bone marrow ≥60%
FLC	sFLC ratio >100
MRI	1 focal lesion by MRI

BM, bone marrow; FLC, free light chain; MRI, magnetic resonance imaging; sFLC, serum free light chain.
Rajkumar et al. *Lancet Oncol.* 2014;15:e538-e548. Kyle et al. *Leukemia* 2010;24:1121-1127.

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Active Myeloma

Not CRAB but now SLiM CRAB

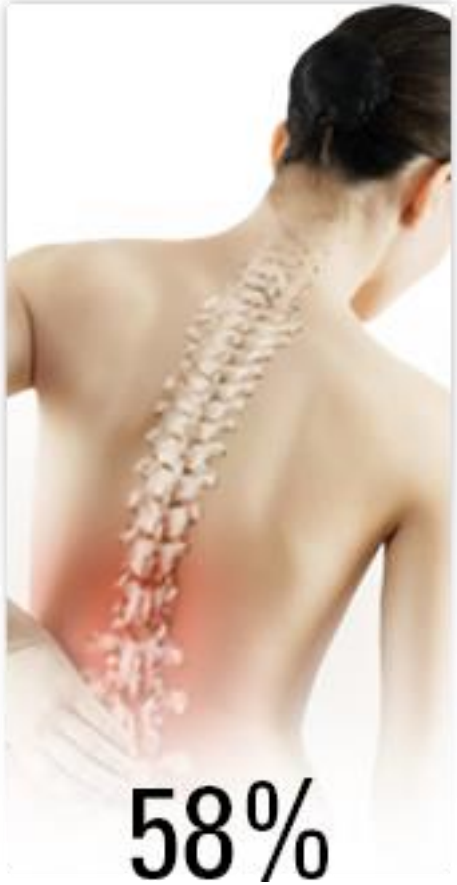
- S (60% Plasmacytosis)
- Li (Light chains I/U >100)
- M (MRI 1 or more focal lesion)
- C (calcium elevation)
- R (renal insufficiency)
- A (anemia)
- B (bone disease)

Rajkumar SV, et al. *Lancet Oncol*. 2014;15:e538-e548.

Multiple Myeloma diagnosis can be challenging

32%

Fatigue



58%

Bone Pain

73%

Anemia

Kyle RA. Mayo Clin Proc. 2003;78:21-33.

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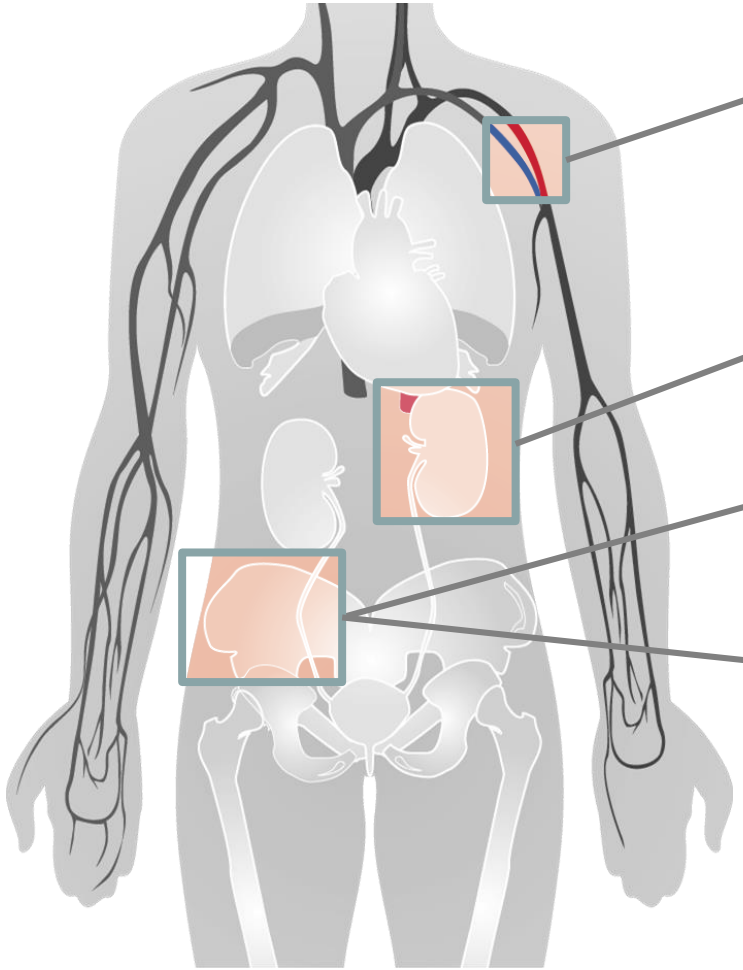
More About the Common "CRAB" Symptoms



Low Blood Counts
- May lead to **anemia** and infection
- **Anemia** is present in 60% at diagnosis

→ **Weakness Fatigue Infection**

Decreased Kidney Function
- Occurs in over half of myeloma patients

→ **Weakness**

Bone Damage
- Affects 85% of patients
- Leads to fractures

→ **Bone pain**

Bone Turnover
- Leads to high levels of **calcium** in blood (hypercalcemia)

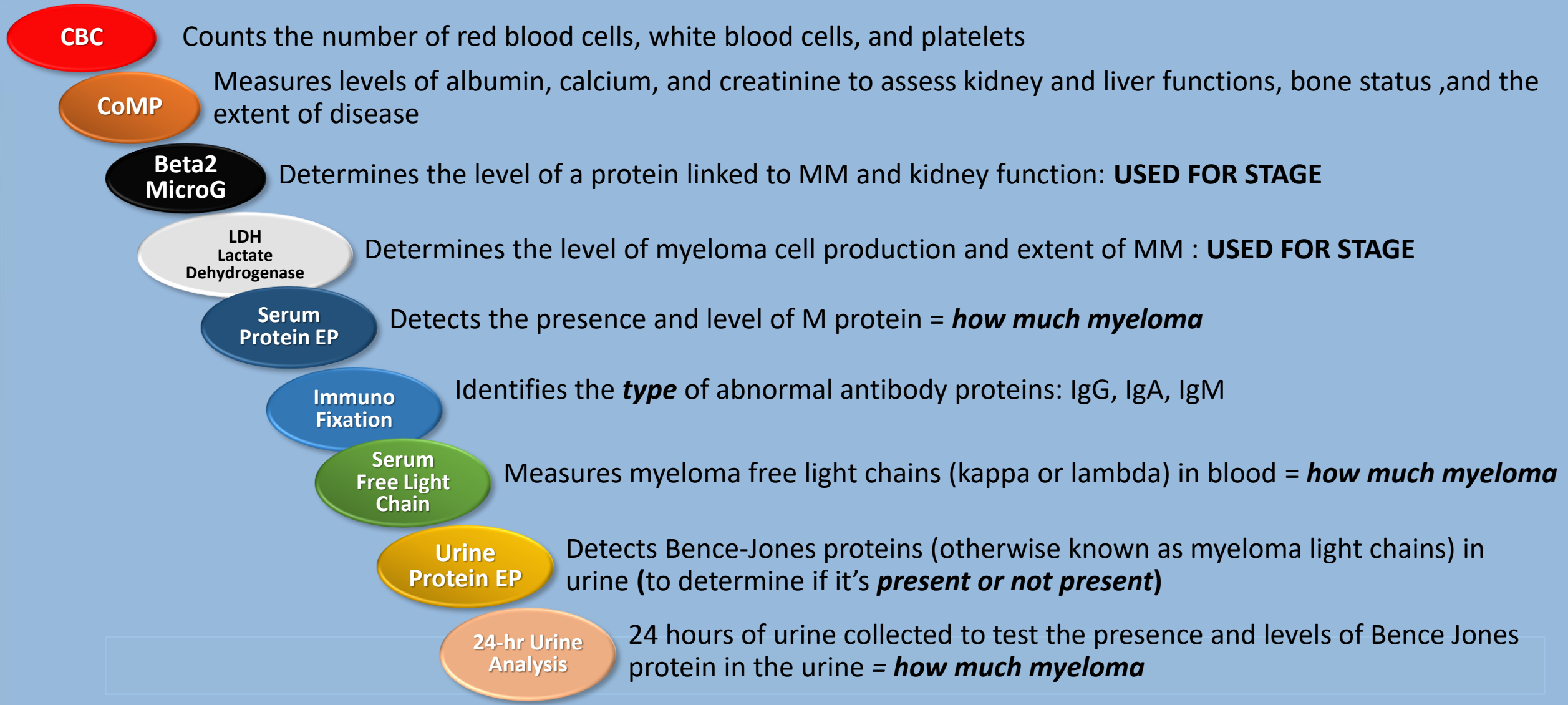
→ **Loss of Appetite & Weight loss**

About 10% to 20% of patients with newly diagnosed myeloma will not have any symptoms.

Multiple Myeloma - Types

- Subtypes of MM are determined based on the kind of abnormal protein
  - IgG – 55%
  - IgA – 25%
  - IgD – 1-2%
  - IgM – 1%
  - Light Chain Disease only – 20%
  - Non Secretors 1-2 %

Learn Your Labs



Myeloma Stage:
Staging refers to the degree to which the cancer has progressed

Stage 1

β2-microglobulin
under 3.6 mg/L

Normal
Lactate Dehydrogenase (LDH)

AND

NO High Risk Cytogenetics (FISH)

Stage 2

β2-microglobulin
Between 3.5 & 5.4mg/L

NO
High Risk Cytogenetics (FISH)

Stage 3

β2-microglobulin over 5.5 mg/L

HIGH
Lactate Dehydrogenase (LDH)

AND/OR

High Risk Cytogenetics (FISH)
Deletion 17th chromosome
Translocation 4th and 14th
Translocation 14th and 16th
Translocation 14th and 20th

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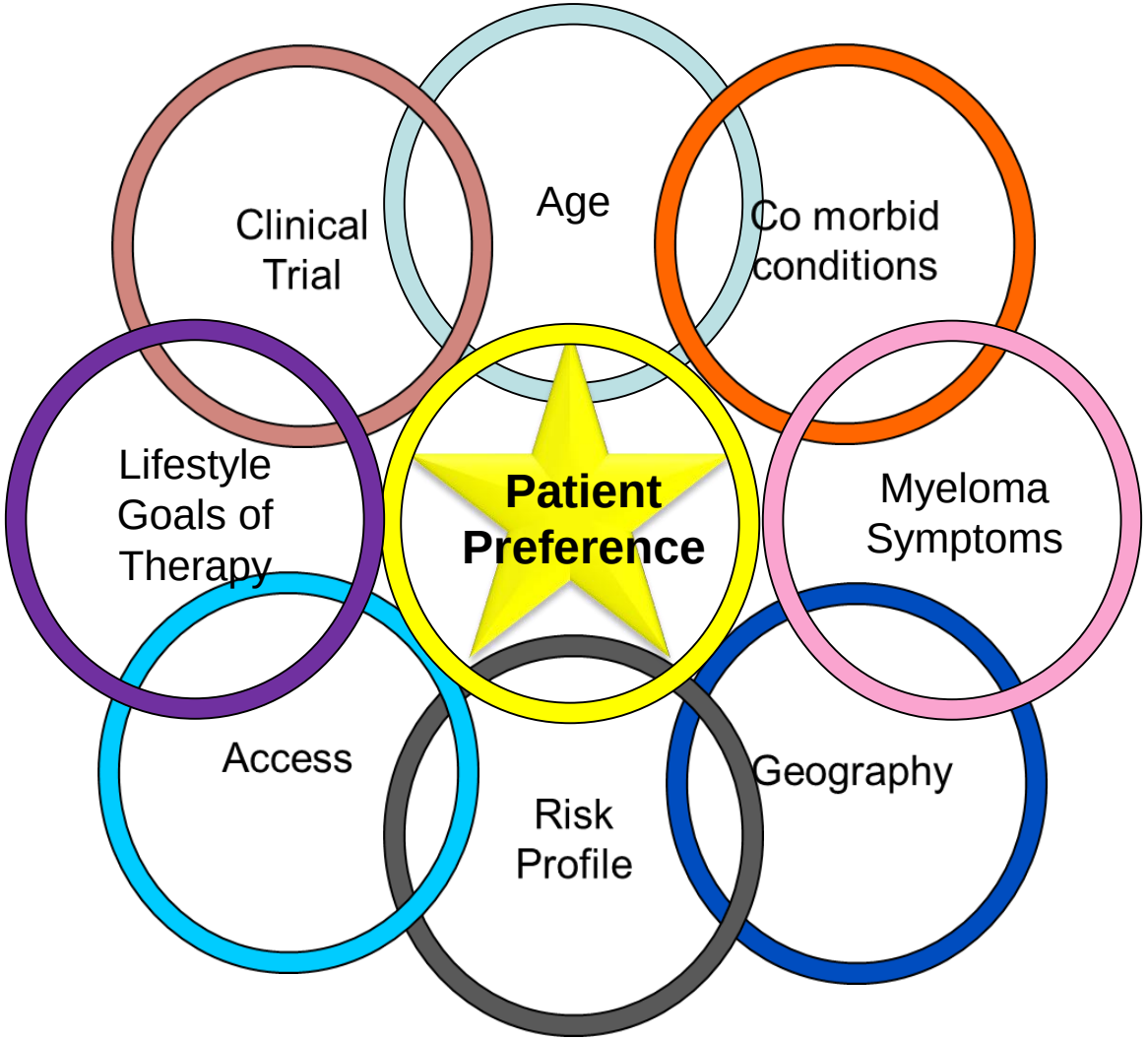
Treatment Planning

Treatment Planning is the process of thinking about the treatment steps you can take with your doctor, based on your goals and preferences. Treatment decisions are based on:

- The results of biomarker tests, cytogenetic (FISH) test, and the stage of multiple myeloma
- Your values, goals, and preferences
- Your age
- Your health and symptoms (if you have kidney disease, heart disease, anemia, or other issues)
- Your medical history and past treatments for multiple myeloma

How to Choose a Treatment Plan



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Tools of the Trade for Frontline Therapy

Standard Drug Overview

Class	Drug Name	Abbreviation	Administration
IMiD immunomodulatory drug	Revlimid (lenalidomide)	R or Rev	Oral
	Thalomid (thalidomide)	T or Thal	
Proteasome inhibitor	Velcade (bortezomib)	V or Vel or B	Intravenous (IV) or subcutaneous injection (under the skin)
	Kyprolis (carfilzomib)	C or K or Car	
	Ninlaro (ixazomib)	N or I	Oral
Chemotherapy	Cytoxan (cyclophosphamide)	C	Oral or intravenous
	Alkeran or Evomela (melphalan)	M or Mel	
Steroids	Decadron (dexamethasone)	Dex or D or d	Oral or intravenous
	Prednisone	P	
Monoclonal Antibodies	Daratumumab (Darzalex)	Dara	Intravenous (IV)

Second/Expert Opinion

- **You have the right** to get a second opinion. Insurance providers may require second opinions.
- A second opinion can help you:
  - Confirm your diagnosis
  - Give you more information about options
  - Talk to other experts
  - Introduce you to clinical trials
  - Help you learn which health care team you'd like to work with, and which facility

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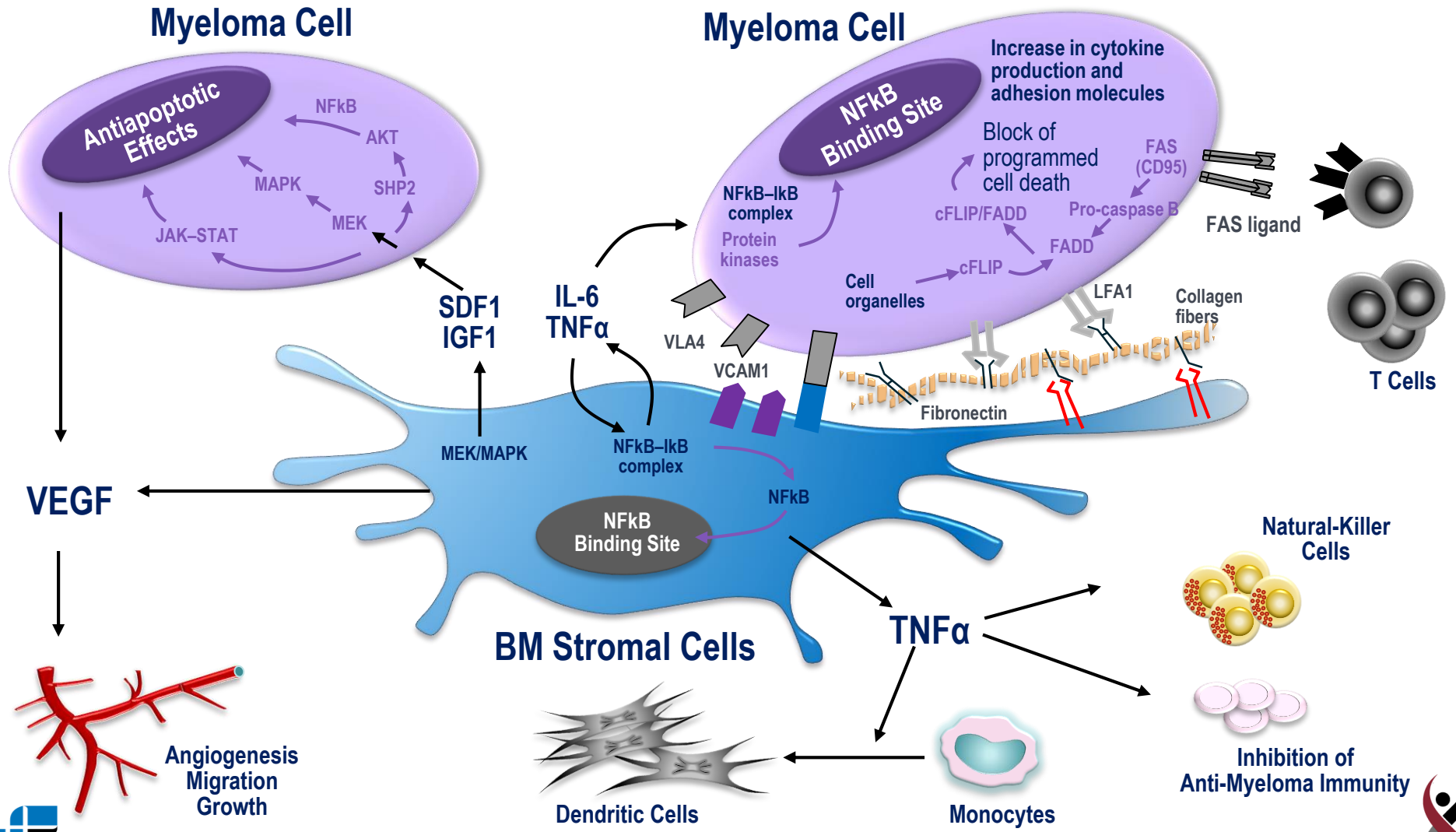
The Myeloma Microenvironment is Key To Disease Pathophysiology



Bruno B et al. Lancet Oncol. 2004;5:430-442.

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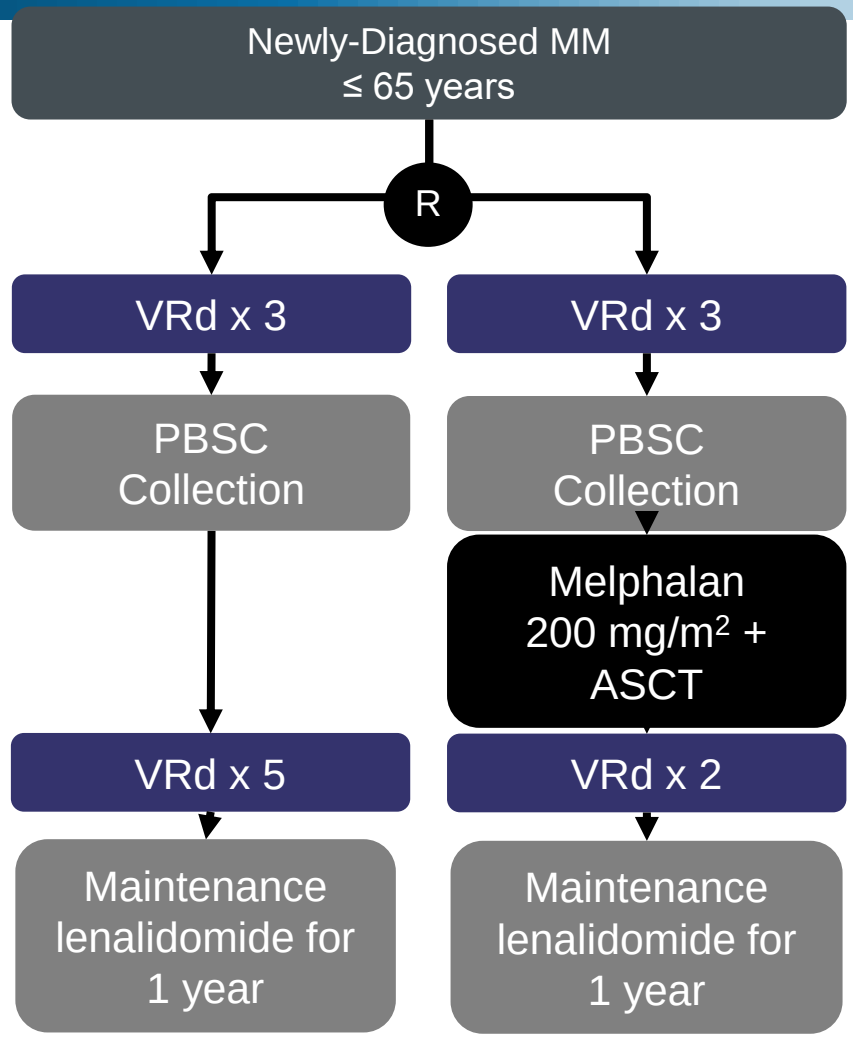
Transplant Eligible

IFM 2009 Study: ASCT vs No ASCT



	VRd Arm	ASCT Arm
n	350	350
CR,* %	48	59
Median PFS,† mo	**36**	**50**
4-year OS, %	82	81

Primary endpoint: PFS; OS data not yet mature.

*P = .03. †P < .001.

Transplant related mortality: 1.7%

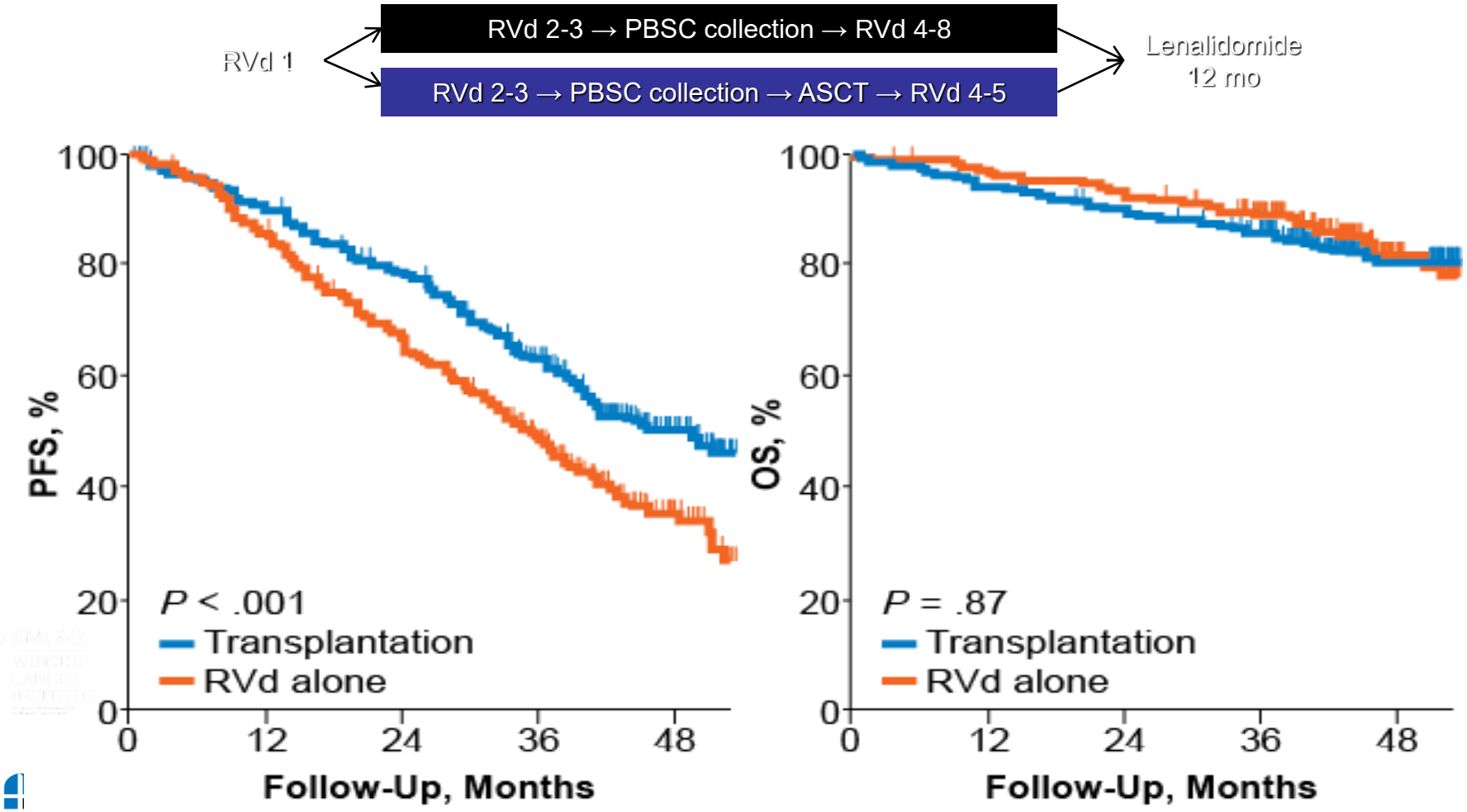
MRD negativity predicted PFS in pooled analysis

ASCT was associated with increased MRD negativity

Regardless of MRD status, PFS was prolonged in the ASCT arm vs the VRd arm

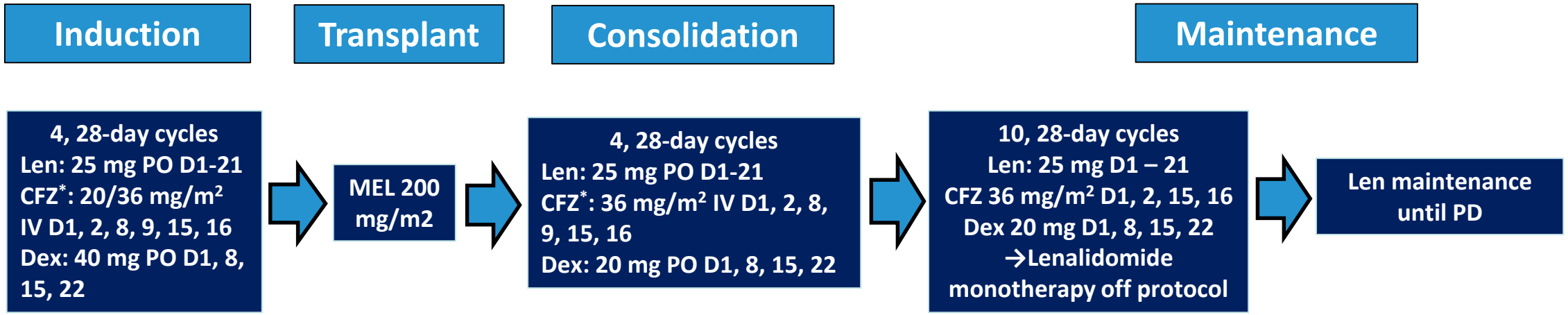
Attal M, et al. *N Engl J Med.* 2017;376:1311-1320.

IFM2009: RVd Alone Vs. RVd + ASCT[1]



1. Attal M et al. *N Engl J Med*. 2017;376:1311-1320

Carfilzomib, Lenalidomide and Dexamethasone (KRD) for Newly-Diagnosed, Transplant-Eligible Multiple Myeloma



Jasielec, J, et al. *Blood* 2020; Epub ahead of print.

GRIFFIN: Phase 2 Study of RVd vs. Dara-RVd in TEMM

Induction Four 21-day Cycles

Consolidation Two 21-day Cycles

Maintenance

RANDOMIZE 1

D-RVd (N = 104)

D 16 mg/kg D1, 8, 15
V 1.3 mg/m^2 IV/SC days 1, 4, 8 and 11
R 25 mg D1 – 14
d 20 mg days 1, 2, 8, 9, 15, 16

ASCT

D-RVd

D 16 mg/kg D1
V 1.3 mg/m^2 IV/SC days 1, 4, 8 and 11
R 25 mg D1 – 14
d 20 mg days 1, 2, 8, 9, 15, 16

D 16 mg/kg
D1 C7 - 32
R D 1 - 21

RVd (N = 103)

V 1.3 mg/m^2 IV/SC days 1, 4, 8 and 11
R 25 mg D1 – 14
d 20 mg days 1, 2, 8, 9, 15, 16

RVd

V 1.3 mg/m^2 IV/SC days 1, 4, 8 and 11
R 25 mg D1 – 14
d 20 mg days 1, 2, 8, 9, 15, 16

R D1 – 21

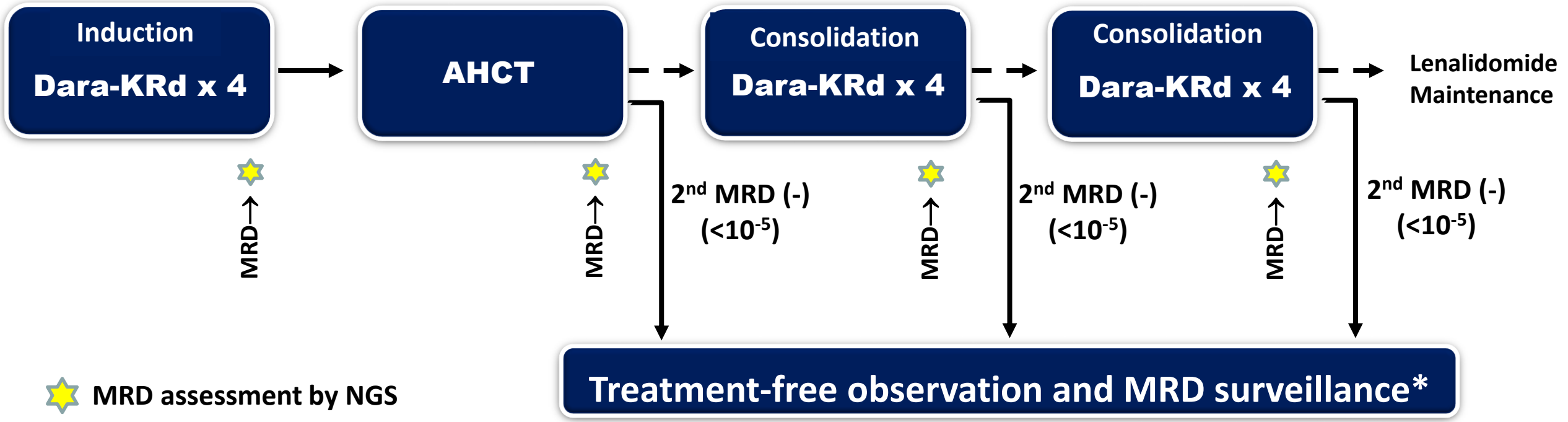
1º Endpoint

- sCR

2º Endpoints

- MRD
- PFS
- OS

MASTER: Phase 2 Study of Dara-KRd in TEMM



Dara-Based Quads: Depth of Response

	N	Post-Induction		Post-ASCT		Post-Consolidation		
		sCR	≥VGPR	sCR	≥VGPR	sCR	≥VGPR	MRD-
VTd	542	6.5%	56.1%	9.4%	67.4%	20.3%	78.0%	43%
D-VTd	542	7.4%	64.9%	13.4%	76.7%	28.9%	83.4%	62%
RVd	103	7.2%	56.7%	14.4%	66.0%	32.0%	72.9%	20.4%
D-RVd	104	12.1%	71.7%	21.2%	86.9%	42.4%	90.9%	51.0%
D-KRd	81	39%	91%	81%	100%	95%	100%	82%

Costa L, et al. ASH 2019.

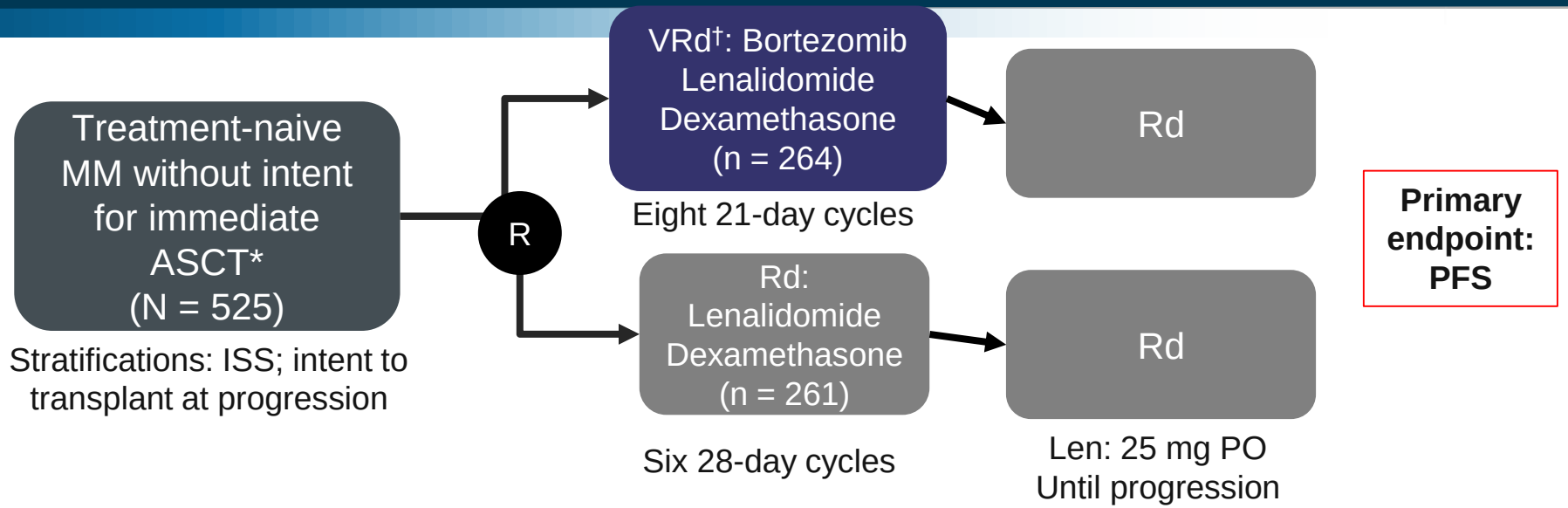
Moreau, P et al. *Lancet* 2019;394:29-38.

Voorhees P, et al. ASH 2019.

Transplant Ineligible

VRd vs Rd: SWOG S0777 Data

3-Drug Regimen as Initial Induction

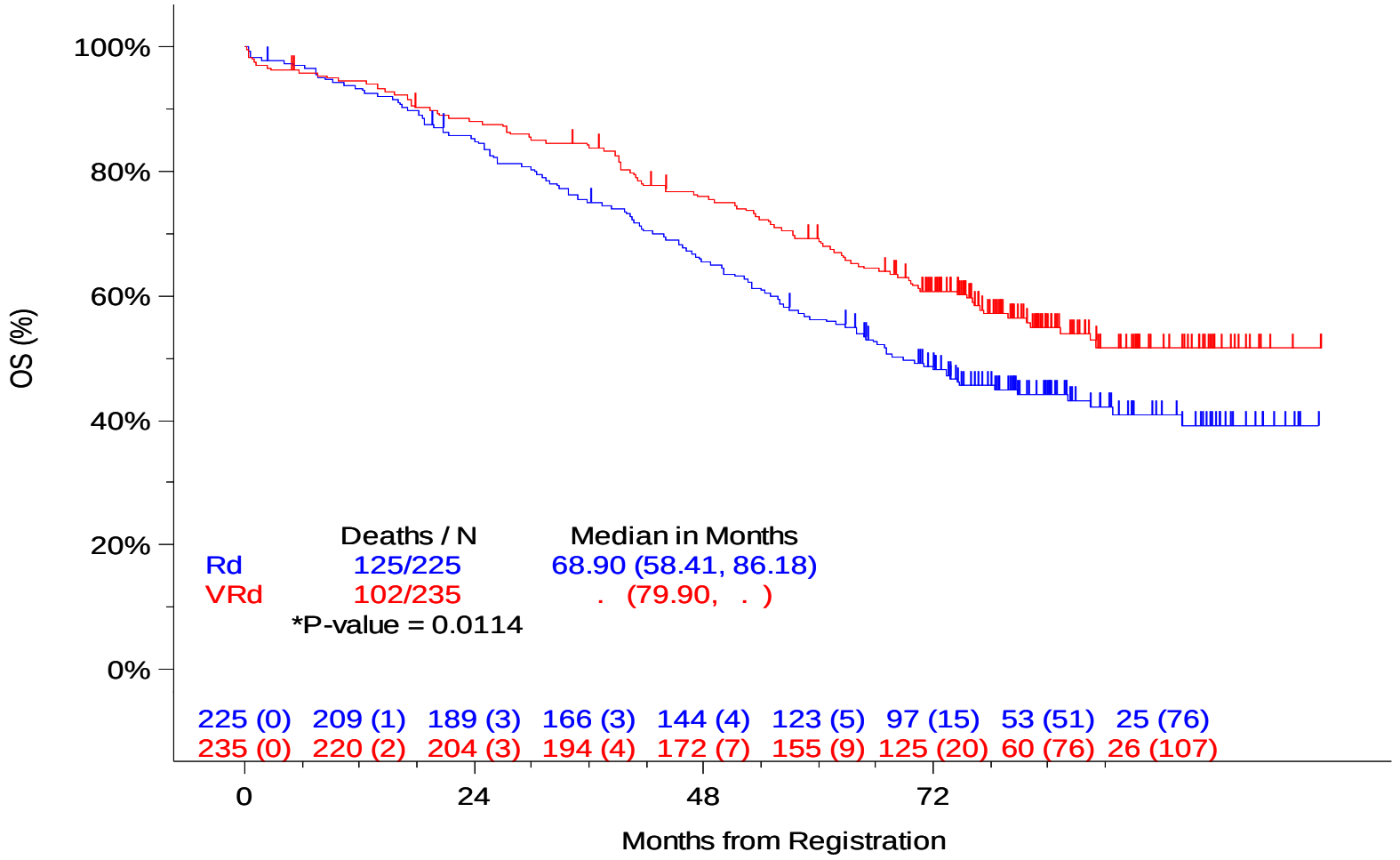


	VRd	Rd	HR; *P* Value
Median PFS, mo	43	30	0.712; .0018 (1-sided)
Median OS, mo	75	64	0.709; .025 (2-sided)

VRd showed better PFS in patients with high- or standard-risk vs Rd‡

- *All patients received aspirin (325 mg/d). †Patients received HSV prophylaxis.
- ‡High-risk cytogenetics included: t(4;14), t(14;16), or del(17p); preliminary data from 316 patients.
- Durie BG, et al. *Lancet.* 2017;389:519-527.

Overall Survival By Assigned Treatment Arm



Durie BG, et al. Blood. 2015;126: Abstract 25. Durie BG, et al. Lancet. 2016 Dec 22 [Epub ahead of print].

VRD is a Standard of Care in Myeloma for Both Eligible and Ineligible Patients

- However, the regimen is limited by the shorter use of bortezomib
  - Study design called for 8 cycles but median was 6 cycles
  - Most common cause of discontinuation was neuropathy

- Mounting evidence supports continuous therapy in transplant ineligible patients

- It would be ideal if we could combine effective and well tolerated agents to treat with a combination for longer…

- There is also a need to consider alternatives when patients have pre-existing neuropathy

The ENDURANCE Trial

Multicenter, randomized (1:1), open-label, phase 3 study (N = 1087)

Key Eligibility Criteria

Standard risk disease

RANDOMIZE 1

VRd

Twelve 21-day cycles = 36 weeks
V 1.3 mg/m^2 IV/SC days 1, 4, 8 and 11 of cycles 1 – 8, days 1 and 8 of cycles 9 – 12
R days 1-21 cycles 1 – 14
d days 1, 2, 4, 5, 8, 9, 11 and 12 cycles 1 – 8, days 1, 2, 8 and 9 of cycles 9 – 12

KRd

Nine 28-day cycles = 36 weeks
K 27 mg/m2 days 1, 2, 8, 9, 15 and 16
R days 1-21
d days 1, 8, 15 and 22

RANDOMIZE 2

4-week cycles x 24
Len days 1 – 21

4-week cycles until PD or unacceptable Toxicity
Len days 1 – 21

1º Endpoint #1

- PFS

1º Endpoint #2

- OS

ClinicalTrials.gov identifier: NCT01863550

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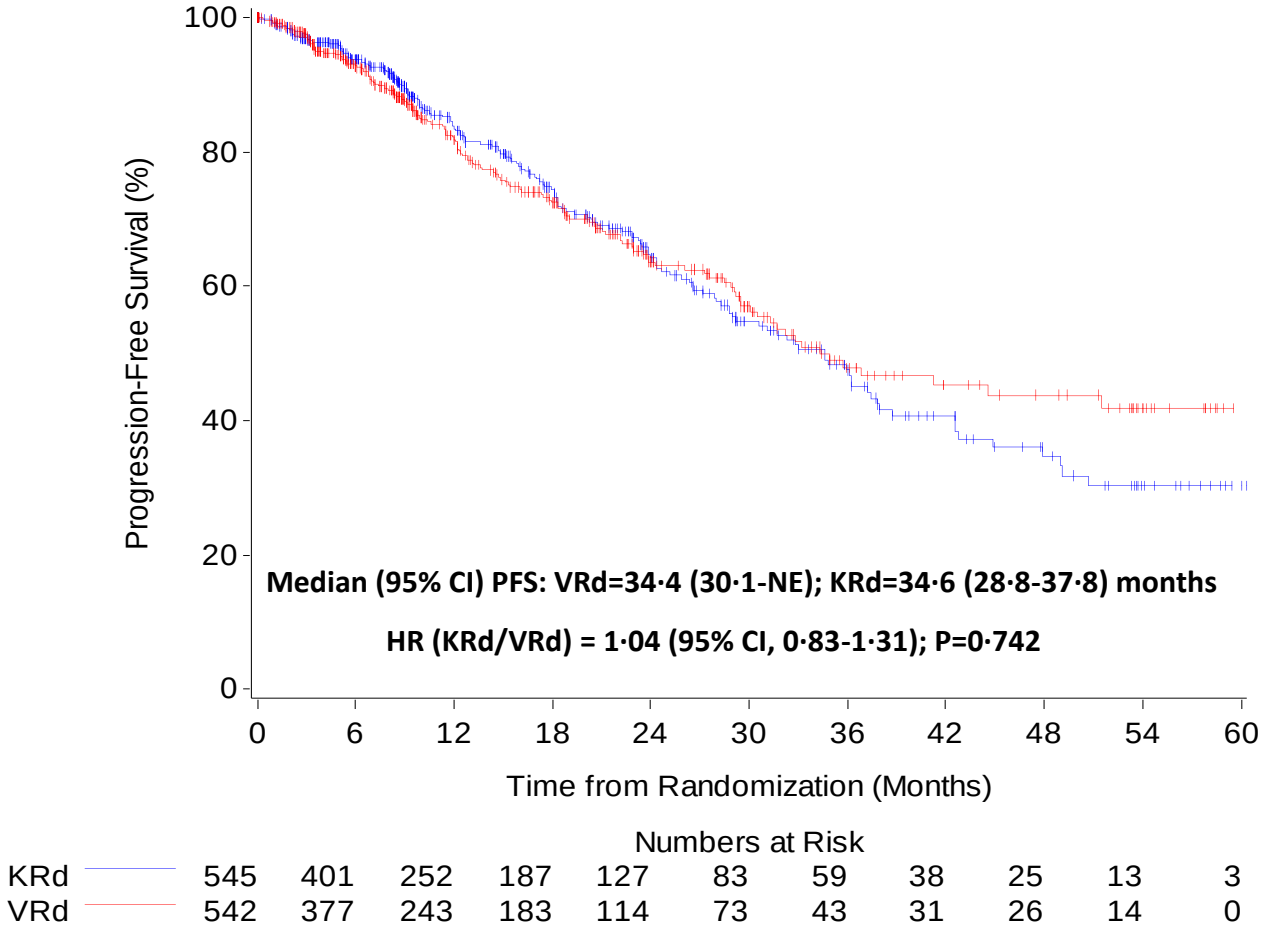
ENDURANCE: PFS

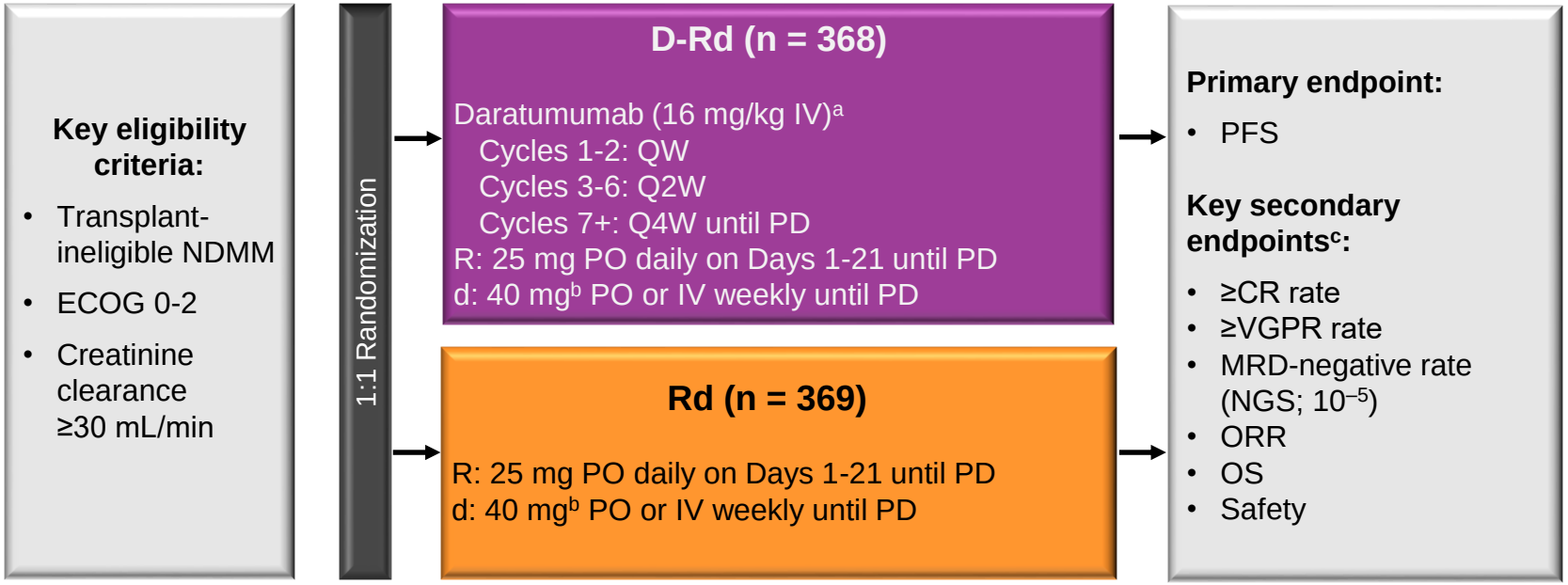


- 2nd interim analysis of PFS (Jan 2020): 298 PFS events (75% of 399 planned)
- Median (95% CI) estimated follow up of 15 (13-18) months
- For patients >/= 70 years, median PFS(95% CI) for VRd = 37 (29-NE) and KRd = 28 (24-36) months
- With censoring at SCT or alternative therapy: Median PFS (95% CI) for VRd = 31·7 (28·5-44·6) and KRd = 32·8 (27·2-37·5) months

Kumar, S, et al. ASCO 2020.

MAIA Study Design

- Phase 3 study of D-Rd vs Rd in transplant-ineligible NDMM (N = 737)



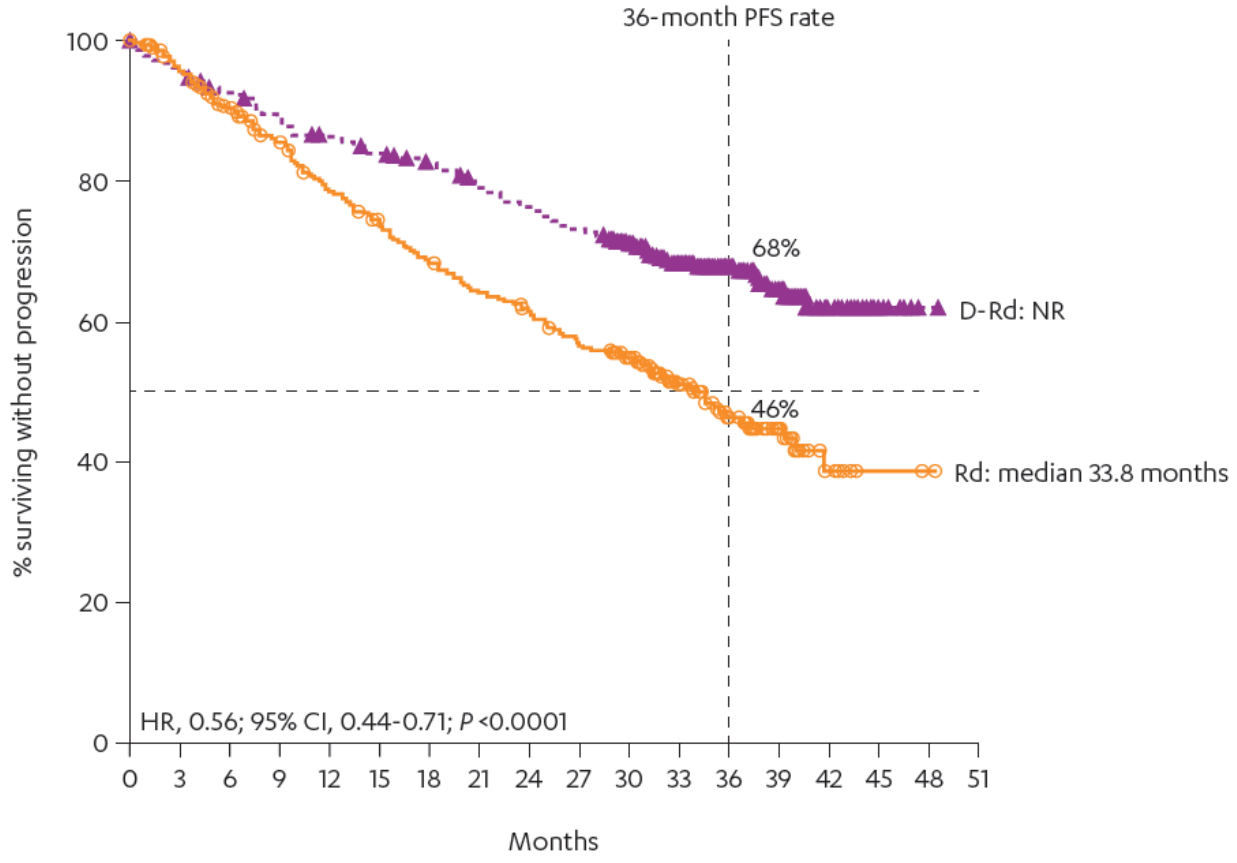
Stratification factors
- ISS (I vs II vs III)
- Region (NA vs other)
- Age (<75 vs ≥75 years)

Cycle: 28 days

[a]On days when daratumumab was administered, dexamethasone was administered to patients in the D-Rd arm and served as the treatment dose of steroid for that day, as well as the required pre-infusion medication.
[b]For patients older than 75 years of age or with BMI <18.5, dexamethasone was administered at a dose of 20 mg weekly.
[c]Efficacy endpoints were sequentially tested in the order shown.

ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; NA, North America; IV, intravenously; QW, once weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; PD, progressive disease; PO, orally; CR, complete response; VGPR, very good partial response; MRD, minimal residual disease; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival; BMI, body mass index.

Efficacy: PFS



Patients at risk

Rd	369	333	307	280	254	236	219	204	194	177	161	113	64	33	10	2	1	0
D-Rd	368	347	335	320	309	300	290	276	266	256	233	174	131	70	24	7	1	0

44% reduction in the risk of progression or death in patients receiving D-Rd

CI, confidence interval., [a]Kaplan-Meier estimate.

Bahlis N, et al. ASH 2019: Abstract 1875

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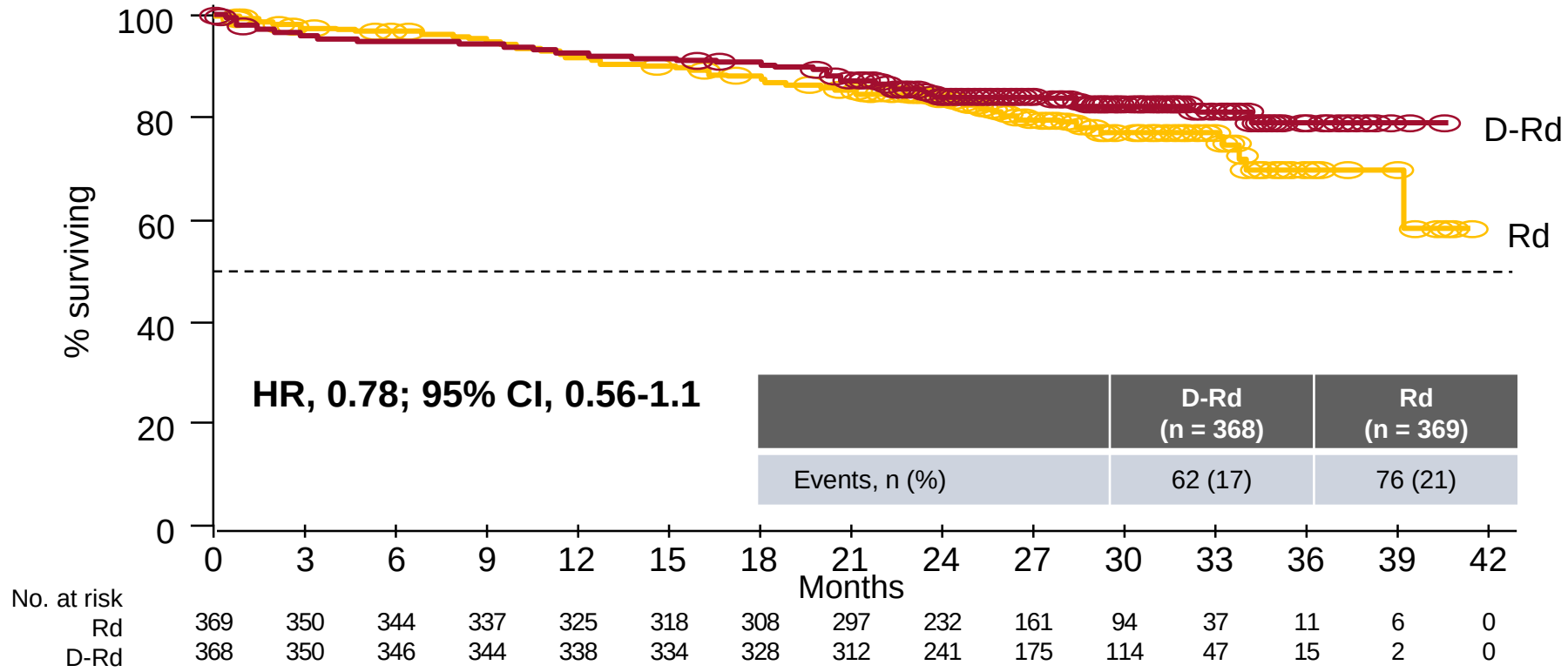
Efficacy: OS at Median Follow-up of 28 Months



	D-Rd (n = 368)	Rd (n = 369)
Events, n (%)	62 (17)	76 (21)

Data are immature after median follow-up of 28 months

Facon T, et al. ASH 2018. Abstract LBA-2.

MAIA: Conclusions

- Addition of daratumumab to Rd reduced risk of progression or death by 44% in patients with ASCT-ineligible newly diagnosed MM
  - Improved depth of response with daratumumab, including 2-fold higher stringent CR/CR rate and 3-fold improvement in MRD negativity

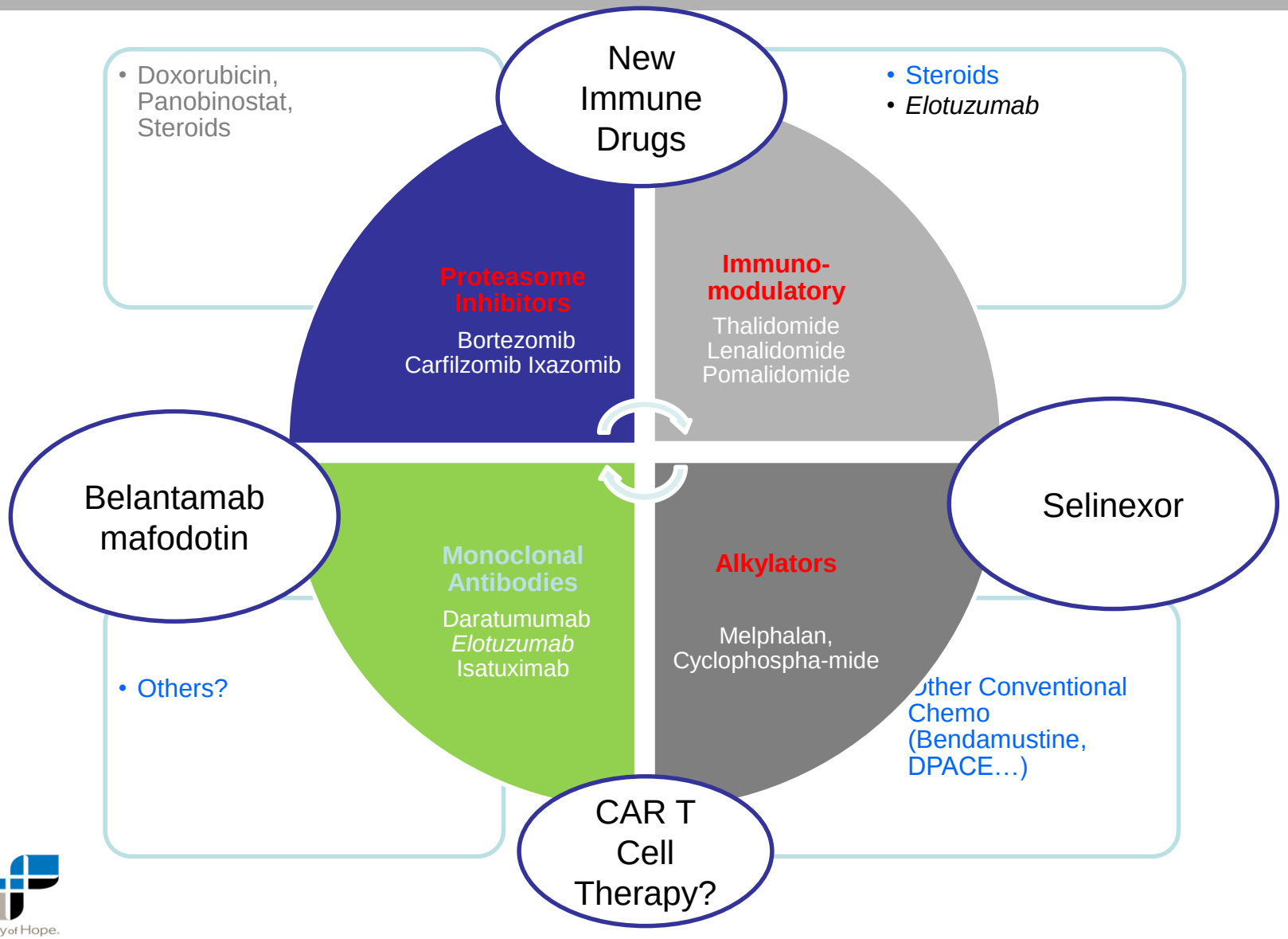
- Safety profile of daratumumab/lenalidomide/dexamethasone in newly diagnosed MM similar to previously reported in R/R MM

Facon T, et al. ASH 2018. Abstract LBA-2.

Conclusions in Transplant Ineligible Patients

- There is more overlap than ever between therapies for transplant eligible and transplant ineligible patients
- Although ASCT remains the standard of care, use is likely to decline in patients who are 65-75 or with significant comorbidities
- Continuous therapy has resulted in better outcomes
- The balance of toxicity and efficacy is particularly important in this population
- My approach is to select 2 agents from the 3 Novel Classes (PIs, IMiDs and MoAbs)
  - I favor DRD in standard risk patients
  - I favor VRD in high risk patients
- DRD is more easily delivered and feasible
- D-VRD may well be a future standard of care

Pillars of Myeloma Treatments



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Options of Therapy for Myeloma - Current

	ASCT eligible	non-ASCT eligible
Induction therapy	Bortezomib-Lenalidomide-Dex OR Carfilzomib-Lenalidomide-Dex ASCT (melphalan) ↓ Lenalidomide Maintenance	Bortezomib-Lenalidomide-Dex OR Lenalidomide-dexamethasone OR Daratumumab-based combination? ↓ Lenalidomide Maintenance
First relapse	Daratumumab-Pomalidomide-Dex Daratumumab-Carfilzomib-Dex Daratumumab-Lenalidomide-Dex Daratumumab-Bortezomib-Dex	
Second Relapse	Carfilzomib Based Combination – Pomalidomide or Cyclophosphamide Pomalidomide Based Combination – Isatuximab or Elotuzumab	
Third Relapse	Selinexor-Dex (+/- bortezomib) Reuse prior therapies in combination	

Caveats – consider second transplant and clinical trials

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Options of Therapy for Myeloma - Future

	ASCT eligible	non-ASCT eligible
Induction therapy	Daratumumab + Bortezomib-Lenalidomide-Dex Carfilzomib-Lenalidomide-Dex	Daratumumab +Bortezomib-Lenalidomide-Dex Lenalidomide-dexamethasone Daratumumab-based combination?
CAR T Cell?	ASCT (melphalan)	
	Lenalidomide Maintenance	Lenalidomide Maintenance
First relapse	Daratumumab-Pomalidomide-Dex Daratumumab-Carfilzomib-Dex Daratumumab-Lenalidomide-Dex Daratumumab-Bortezomib-Dex	
BCMA Antibody + IMid + PI Selinexor + PI +/- IMiD		
Second Relapse	Carfilzomib Based Combination – Pomalidomide or Cyclophosphamide Pomalidomide Based Combination – Isatuximab or Elotuzumab	
Belantamab +/- CAR T Cell? Melflufen?		
Third Relapse	Selinexor-Dex (+/- bortezomib) Reuse prior therapies in combination	
Bispecific and Trispecific Abs?		

Caveats – consider second transplant and clinical trials

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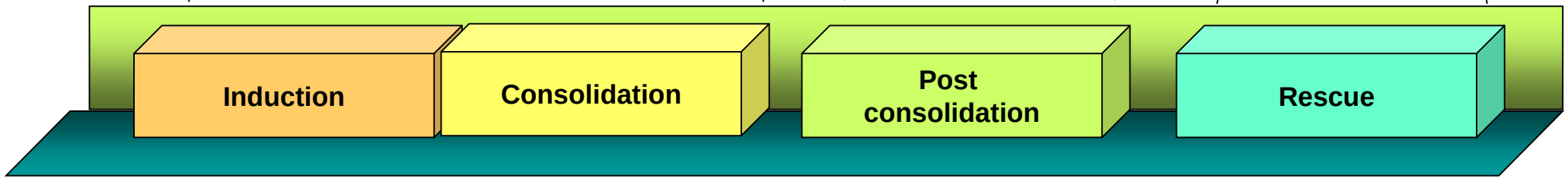
The Evolution of Myeloma Therapy

Now

Front line treatment		Maintenance	Relapsed
VD	SCT	Nothing	Bortezomib Panobinostat
Rev/Dex	Tandem ASCT (?)	Thalidomide?	Lenalidomide Daratumumab
CyBorD		Bortezomib	Thalidomide Ixazomib
VTD		Ixazomib	Carfilzomib Elotuzumab
VRD		Lenalidomide	Pomalidomide Selinexor
KRD		Combinations	Belantamab mafodotin
D-VMP			
DRD			



New

D-VRD	"more" induction	Daratumumab?	CAR T Cell Therapy
Isa-VRD	Lenalidomide 2 mths	Lenalidomide + PI	Venetoclax
D-KRD			Bispecific/Trispecific Antibodies
Isa-VRD			Cell Modifying Agents
			Melphalan flufenamide
			PD/PDL-1 Inhibition
			Multiple small molecules
			++++++++

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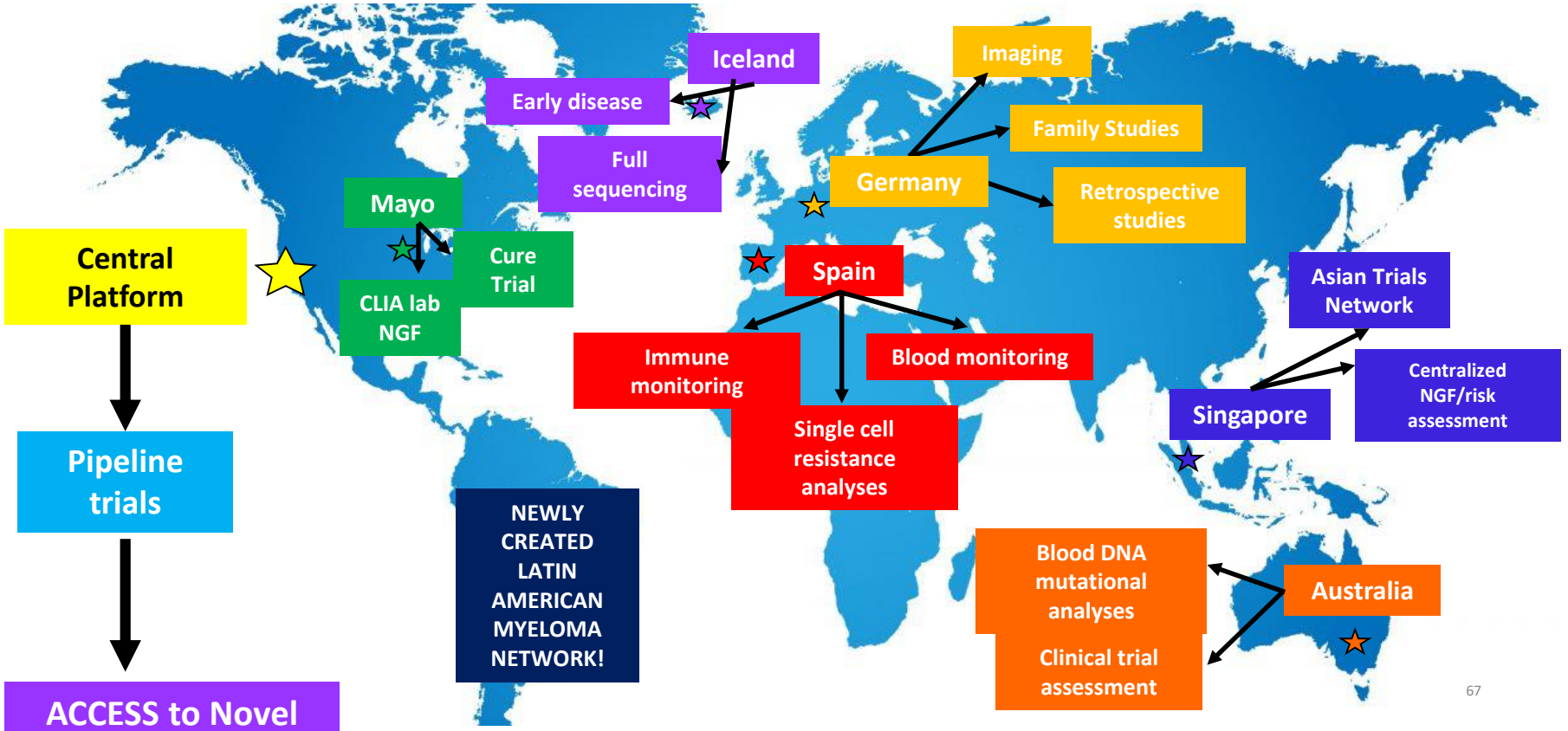
IMF Global Presence

Primary Goal is to cure Myeloma



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Patients
Providers
Countries
Industry
Myeloma Community

BLACK SWAN RESEARCH INITIATIVE

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THANK YOU!

Joseph Mikhael, MD, MEd, FRCPC

Professor, Translational Genomics Research Institute (TGen)
City of Hope Cancer Center

Chief Medical Officer, International Myeloma Foundation

Director of Myeloma Research and Consultant Hematologist, HonorHealth Research Institute

jmikhael@myeloma.org

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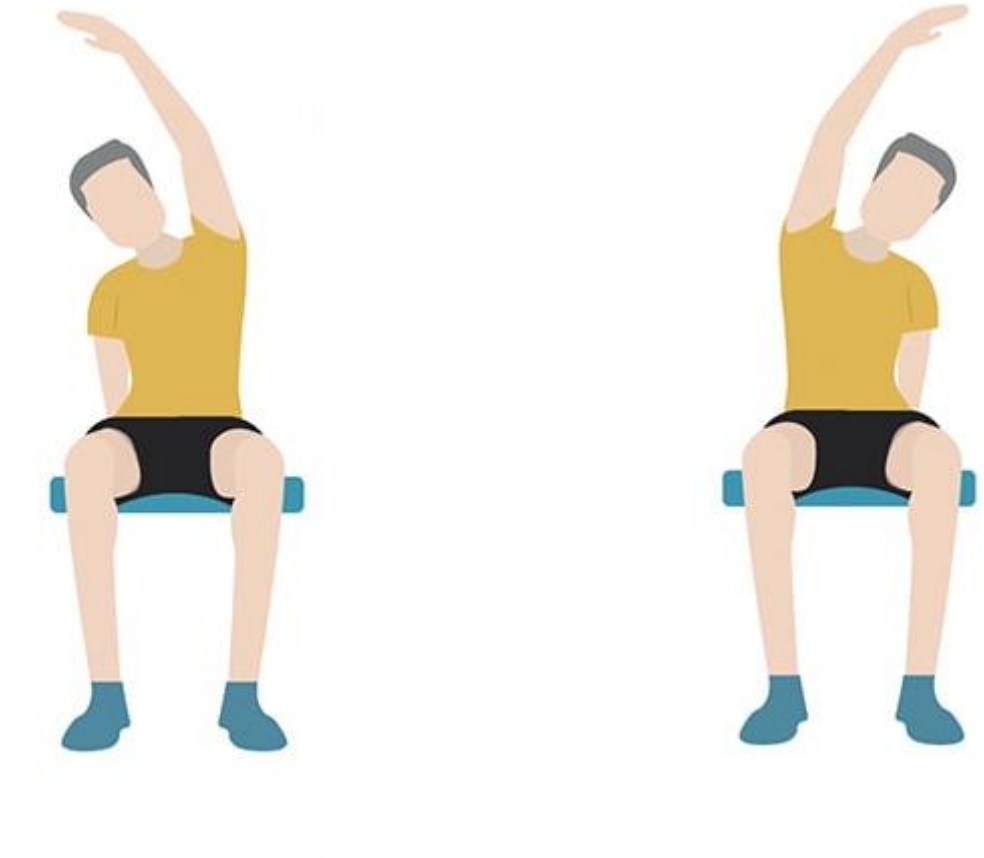
INTERNATIONAL MYELOMA FOUNDATION

REGIONAL
COMMUNITY WORKSHOP

5 Minute Stretch



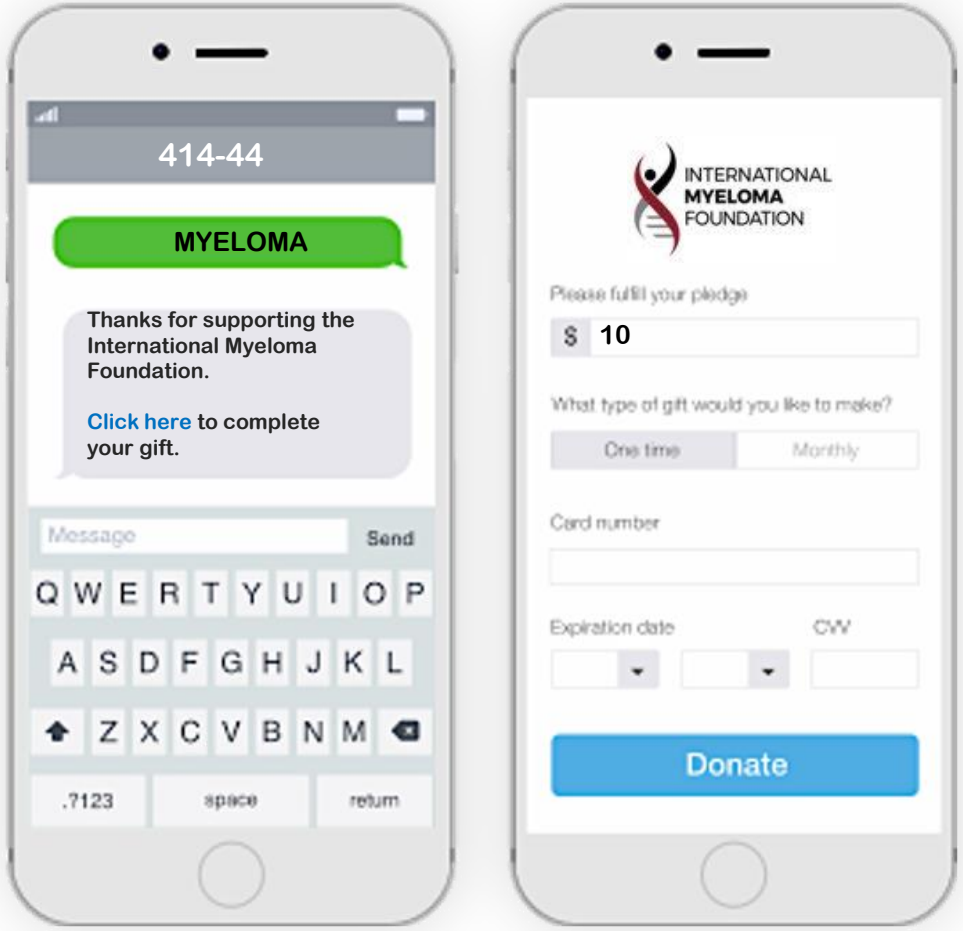
REGIONAL
COMMUNITY WORKSHOP

Giving Tuesday: Text To Give

This #GivingTuesday 12/1/2020, you can MAKE A DONATION to the IMF From Your Smartphone

Step 1 Send a new text message to 41444
Step 2 Text MYELOMA
Step 3 Click the reply message to make a donation

Or scan the below QR code with your smart phone:



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Improving Lives. **Finding the Cure.**

“Relapsed Therapy”
“Emerging Therapies and Clinical Trials”

Nina Shah, MD
University of California, San Francisco (UCSF)

REGIONAL COMMUNITY WORKSHOP

Multiple Myeloma: Relapsed Therapy, Emerging Therapies and Clinical Trials

Nina Shah, MD

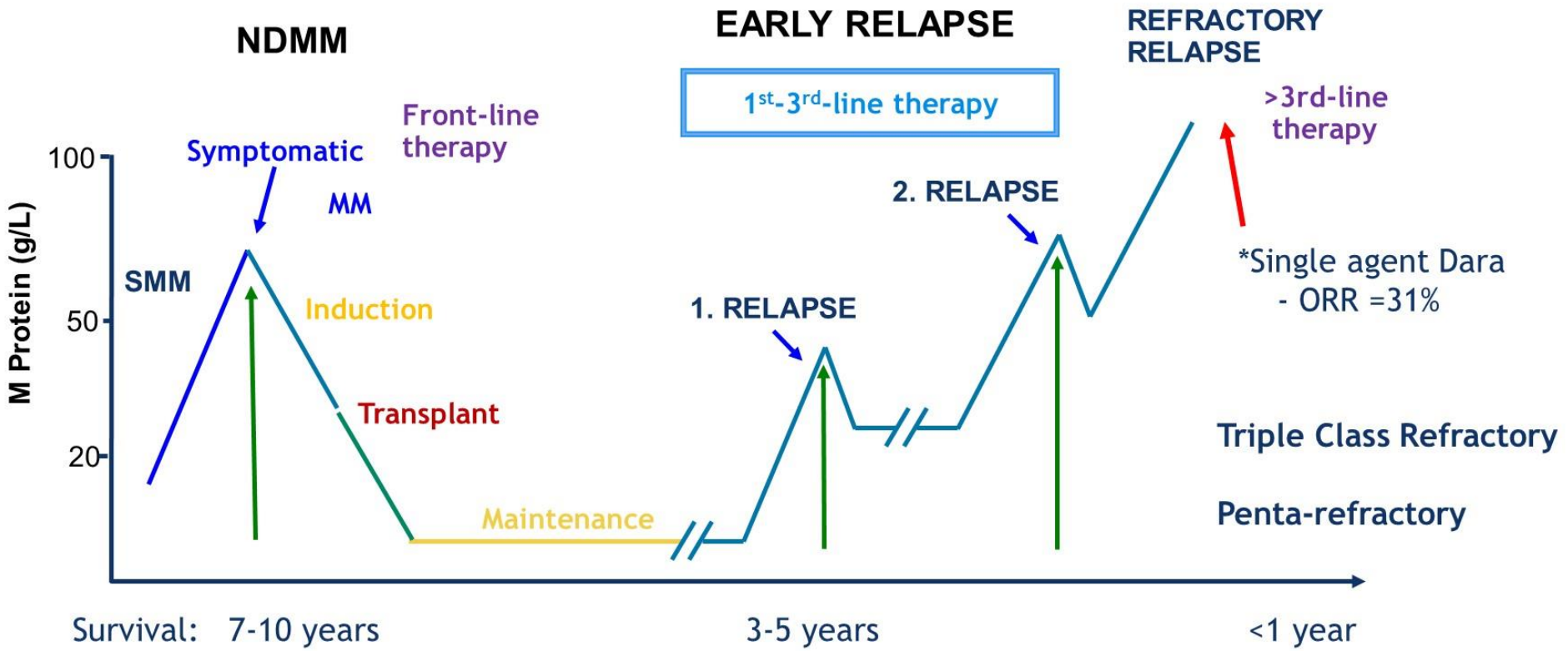
Professor of Clinical Medicine

Multiple Myeloma Translational Initiative

Division of Hematology-Oncology

University of California San Francisco

Natural History in Multiple Myeloma

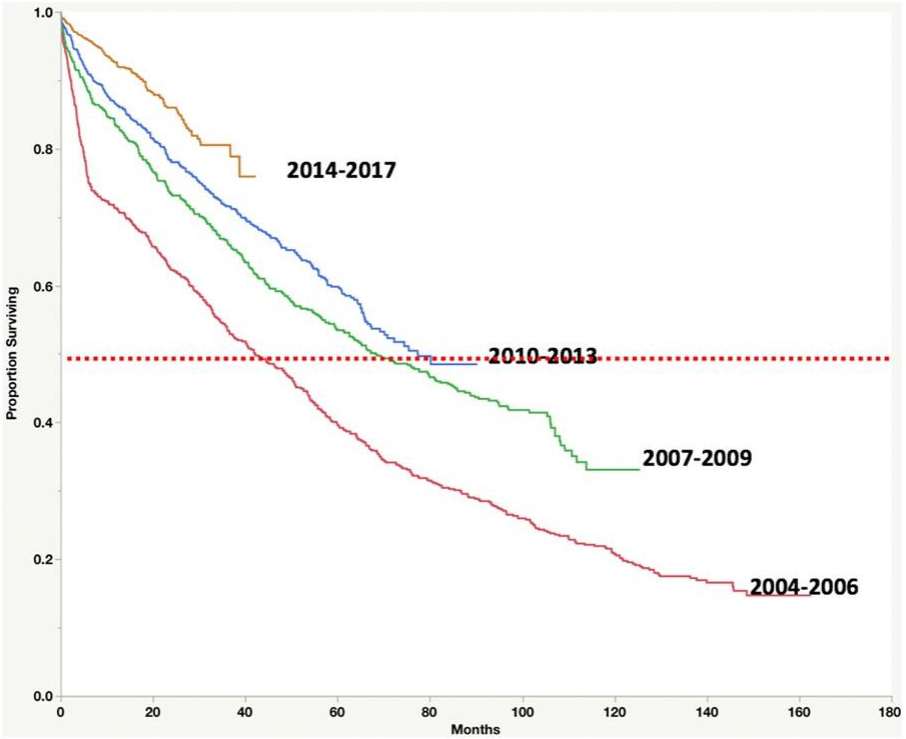


Slide credit: Tom Martin MD

UCSF

Discussion topics

- PI/IMID combinations
- Monoclonal antibodies
- Cell mods
- Antibody drug conjugates
- Bispecifics



Courtesy of Shaji Kumar; adapted from Kumar S. Leukemia (2014) 28, 1122–1128.

Randomized Studies With Lenalidomide-Dexamethasone Control Arms

	Carfilzomib*		Elotuzumab		Daratumumab		Ixazomib	
N	KRd vs Rd 792		ERd vs Rd 646		DRd vs Rd 569		IRd vs Rd 722	
Efficacy	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**
Median follow up, mos	67		Min 48 mos		32.9		23	
ORR	87.1%	66.7%	79%	66%	93%	76%	78.3%	71.5%
CR	32%	9.3%	5%	9%	55%	23%	12%	7%
Median PFS, mos	26	16.6	19	14.9	NR	17.5	21	14.7
PFS HR (95% CI)	0.69 (0.57–0.83)		0.71 (0.59–0.86)		0.44 (0.34–0.55)		0.74 (0.59–0.94)	
Median OS, mos	48.3	40.4	48.3	39.6	NR	NR	NR	NR
OS HR (95% CI)	0.79 (0.67–0.95)		0.78 (0.63–0.96)		NR		NR	

PFS benefit can translate into OS benefit with adequate follow up (though drug access at relapse confounding issue).

Dimopoulos MA et al. *N Engl J Med*. 2016;375:1319; Dimopoulos MA et al. *Br J Haematol*. 2017;178:896; Stewart AK et al. *N Engl J Med*. 2015;372:142; Stewart AK et al. *Blood*. 2017;130: Abstract 743.; Dimopoulos M et al. *J Hematol Oncol.* 2018;11:49; Moreau P et al. *N Engl J Med*. 2016;374:1621.

Slide credit: Ajai Chari MD

UCSF

Randomized Studies With Bortezomib-Dexamethasone Control Arms

	Pomalidomide		Daratumumab*		Carfilzomib		Panobinostat		Elotuzumab†	
N	PVd vs Vd 559		DVd vs Vd 498		Kd vs Vd 929		FVd vs Vd 768		EVd vs Vd 152	
Efficacy	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**
Median follow up, mos	16		26.9		37.5		NR		15.9	
ORR	82%	50%	85%	63%	76%	63%	55%	61%	66%	63%
CR	16%	4%	30%	10%	13%	6%	11%	6%	4%	3%
Median PFS, mos	11	7	16.7	7.1	18.7	9.4	12	8.08	9.7	6.9
PFS HR (95% CI)	0.61 (0.49–0.77)		0.32 (0.25–0.40)		0.53 (0.44–0.65)		0.63 (0.52–0.76)		0.72 (0.59–0.88)	
Median OS, mos	NR	NR	NR	NR	47.6	40.0	40.3	35.8	NR	NR
OS HR (95% CI)	NR		NR		0.79 (0.65–0.96)		0.94 (0.78–1.14)		0.61 (0.32–1.15)	

PFS benefit can translate into OS benefit with adequate follow up (though drug access at relapse confounding issue).

Richardson PG et al. *J Clin Oncol*. 2018;36: Abstract 8001 Palumbo A et al. *N Engl J Med*. 2016;375:754; Spencer A et al. *Haematologica.* 2018; Sep 20 [epub ahead of print]; Dimopoulos MA et al. *Lancet Oncol*. 2016;17:27; San Miguel JF et al. *Lancet Oncol*. 2014;15:1195; Jakubowiak AJ et al. *Blood*. 2016;127:2833.;.

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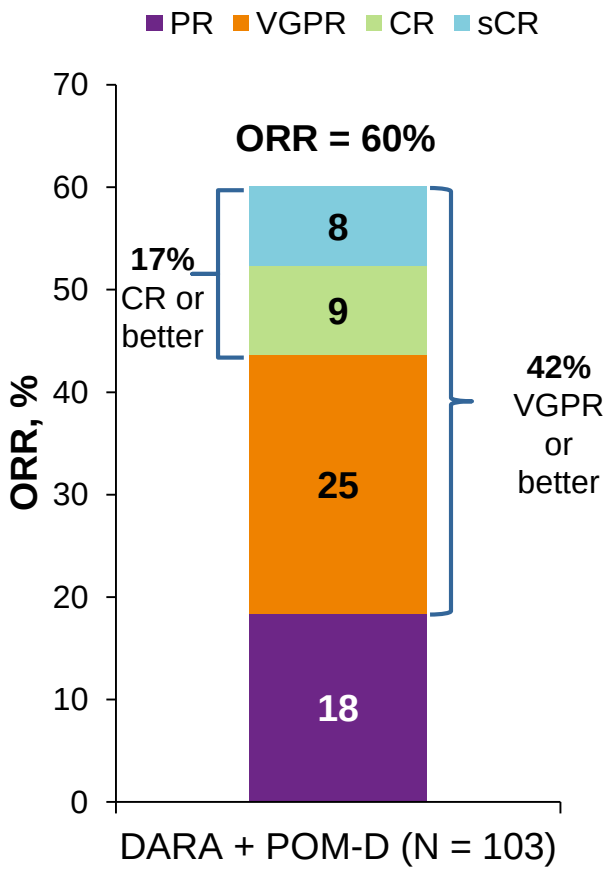
Slide credit: Ajai Chari MD

Triplets are superior to doublets!

What should you use for lenalidomide exposed versus refractory patients?

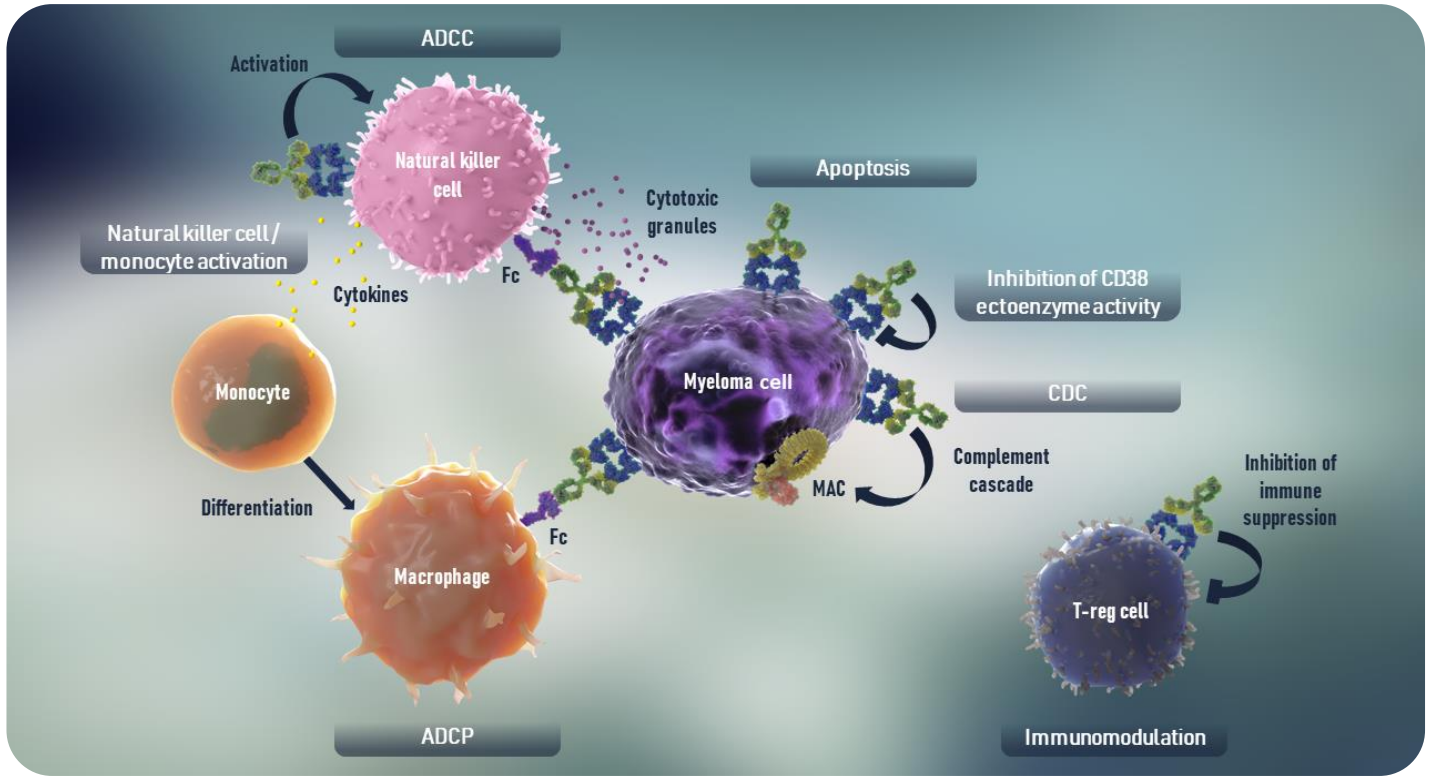
DARA + POM-D



- DARA can be combined with POM-D
  - 77% Gr 3/4 neutropenia in population with 44% baseline neutropenia
  - FN rates consistent with POM-D alone
- DARA (16 mg/kg) + POM-D induced responses, including MRD negativity, in a heavily pretreated patient population
  - Median of 4 prior lines of therapy
  - **89% len refractory**
  - 71% of patients were double refractory to a PI and an IMiD
  - High ORR maintained in double-refractory & high-risk patients
- Median PFS 9.9 mos
- Median OS 17.5 months encouraging

Chari A, et al. Blood. 2017.

Isatuximab: an IgG1 monoclonal antibody targeting CD38



CD38 functions as a receptor and an ectoenzyme, and is highly and uniformly expressed on multiple myeloma cells[1–3]

Isatuximab is an IgG1 monoclonal antibody that targets a specific epitope on the CD38 transmembrane glycoprotein[4,5]

The clinical significance of these findings is currently under investigation

ADCC, antibody dependent cellular cytotoxicity; ADCP, antibody dependent cellular phagocytosis; CDC, complement dependent cytotoxicity; Ig, immunoglobulin; MAC, membrane attack complex

1. Lin P, et al. Am J Clin Pathol. 2004;121:482–8;
2. van de Donk NWCJ, et al. Immunol Rev. 2016;270:95–112;
3. Costa F, et al. Oncotarget. 2017;8:56598–611;
4. Deckert J, et al. Clin Cancer Res. 2014;20:4574–83;
5. Jiang H, et al. Leukemia. 2016;30:399–408

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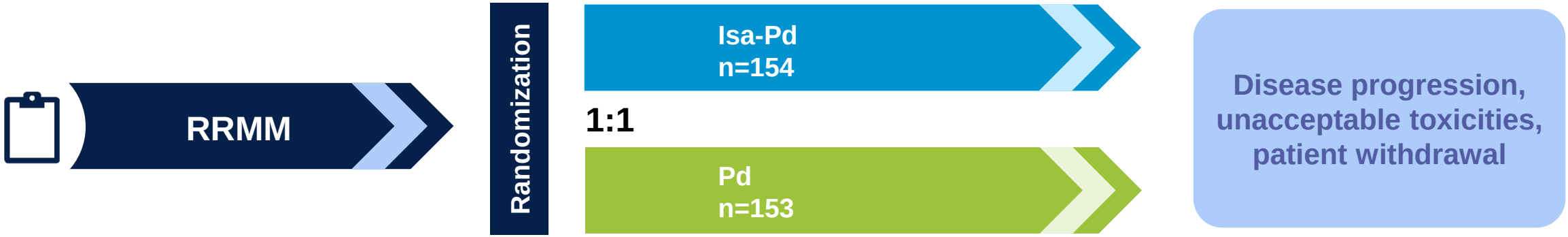
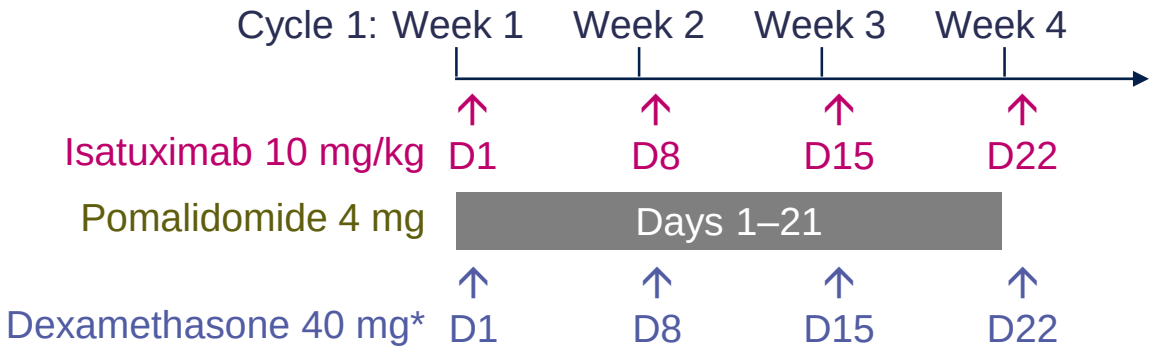
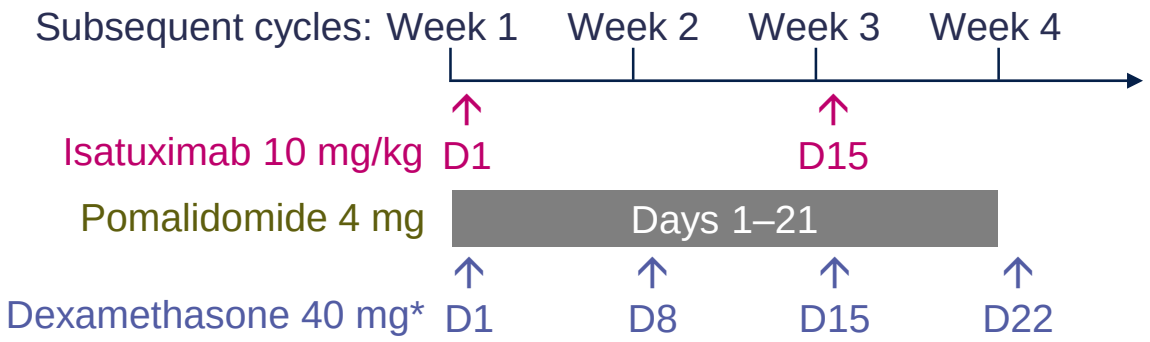
Study design



Sample size calculation: ~300 patients required to detect an HR of 0.6 with 90% power and 1-sided type 1 error of 2.5%





*Dexamethasone dose was 20 mg in patients aged ≥75 years
d, dexamethasone; HR, hazard ratio; Isa, isatuximab; P, pomalidomide; RRMM, relapsed/refractory multiple myeloma

Richardson PG, et al. Future Oncol 2018;14:1035–47;

Attal et al, Lancet 2019

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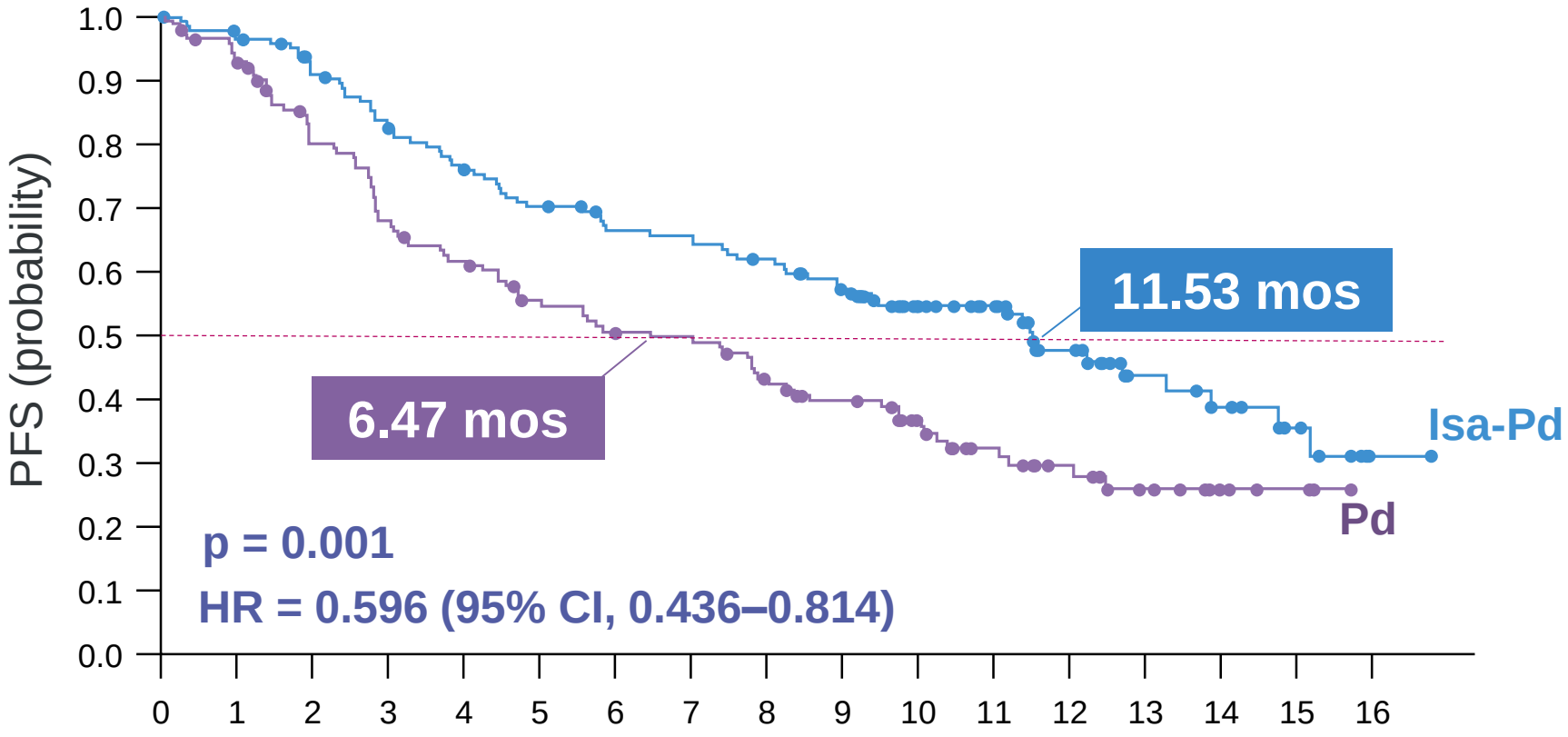
ICARIA: Isa-Pd vs Pd
PFS (IRC assessment – primary endpoint)



No. at risk									
Isa-Pd	154	129	106	89	81	52	30	14	1
Pd	153	105	80	63	51	33	17	5	0

Statistically significant improvement in PFS

Data cut-off 11 Oct, 2018
CI, confidence interval; d, dexamethasone; HR, hazard ratio; IRC, Independent Review Committee; Isa, isatuximab;, mos, months; PFS, progression-free survival; P, pomalidomide

Attal et al, Lancet 2019

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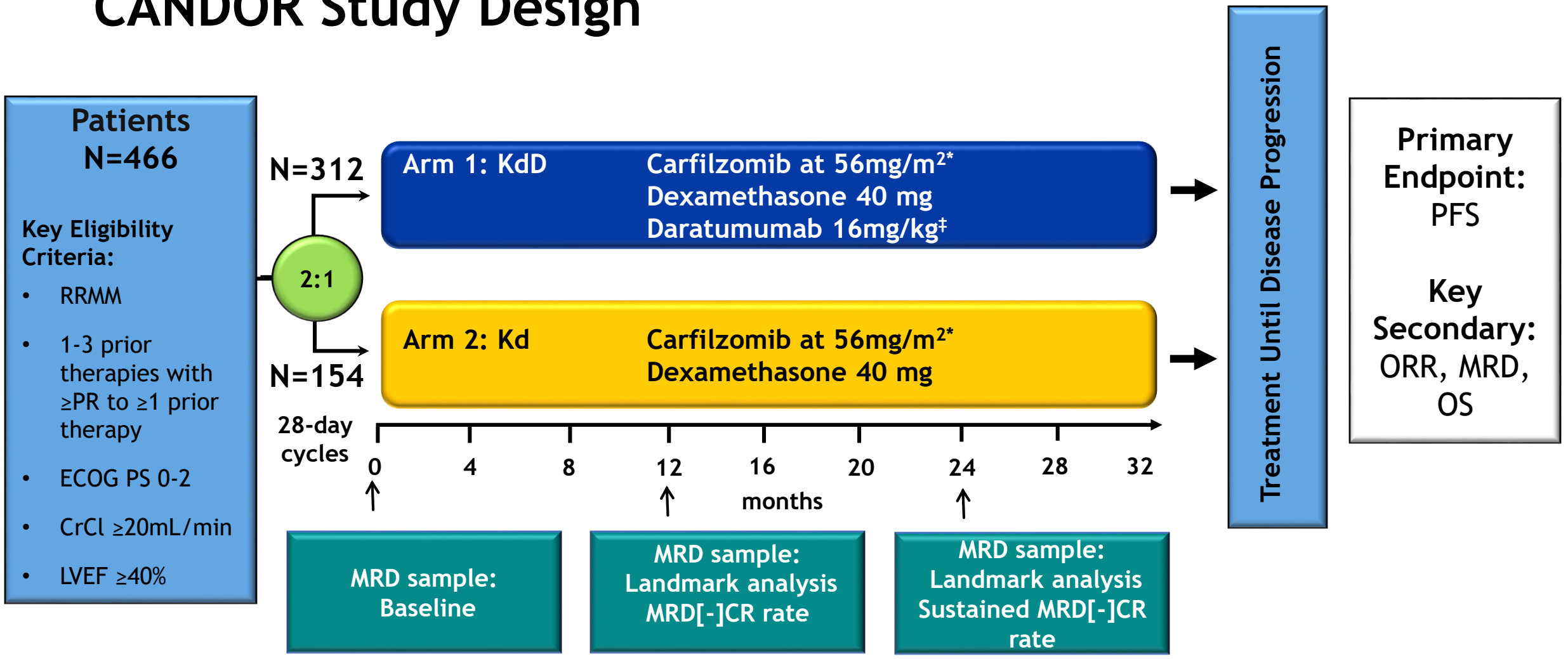
What about going all out…?

Anti-CD38 + carfilzomib

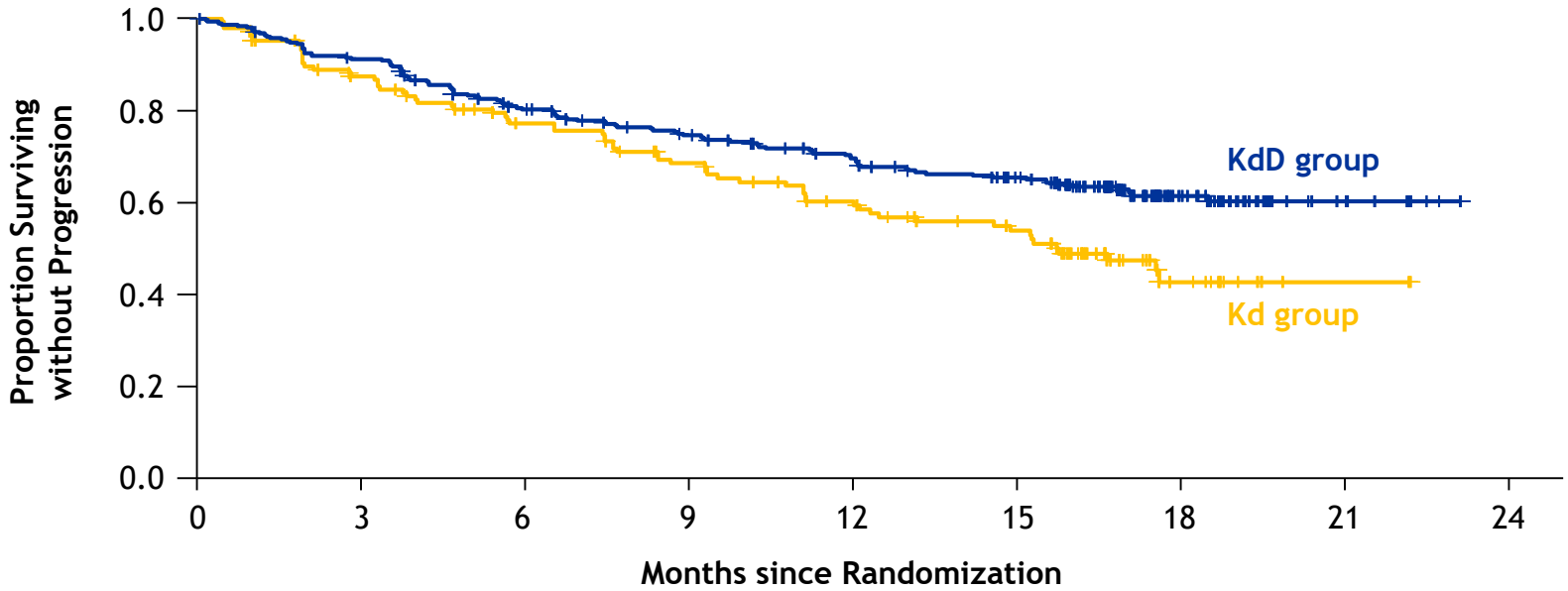
CANDOR Study Design



*Carfilzomib at 56 mg/m^2 administered twice weekly; 20 mg/m^2 administered on days 1 and 2 of cycle 1 only
‡The first dose of daratumumab is split over two days (8 mg/kg each).
CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LVEF, left ventricular ejection fraction; PD, progressive disease; RRMM, relapsed or refractory multiple myeloma

Usmani et al, ASH 2019; Dimopoulos et al, *Lancet* 2020

Primary Endpoint Met: KdD Significantly Prolonged PFS Compared With Kd



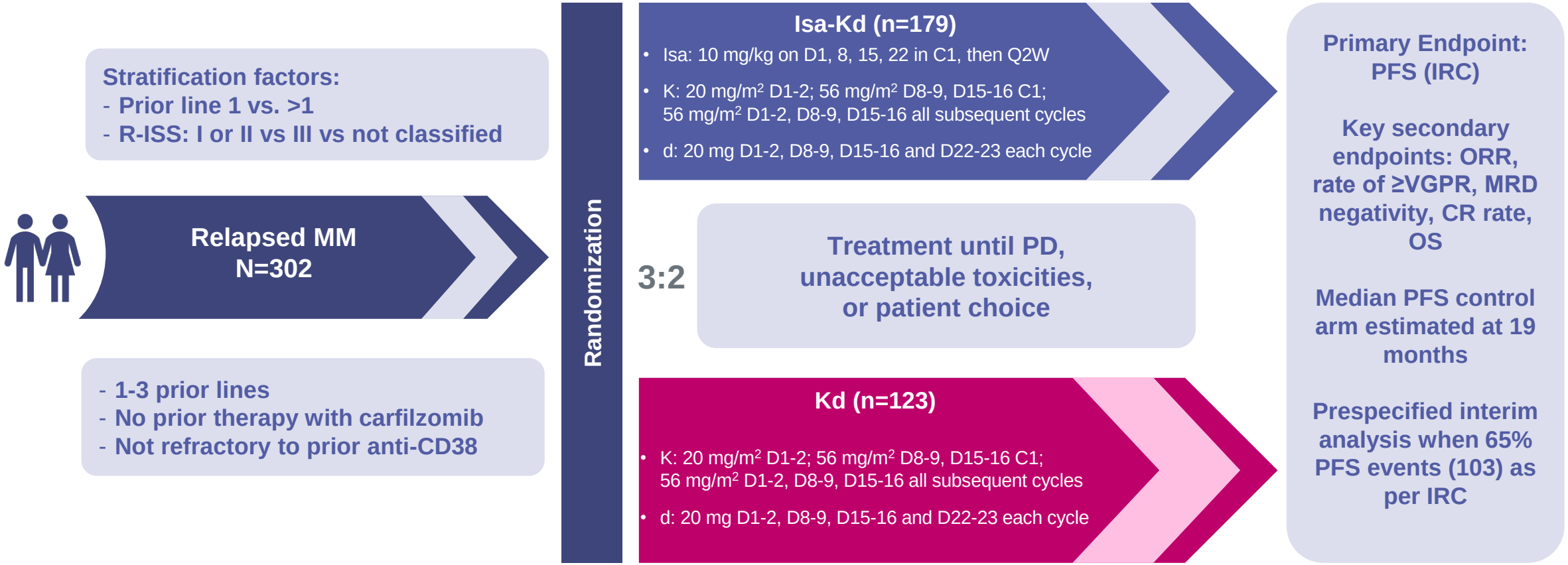
No. at Risk									
KdD group	312	279	236	211	189	165	57	14	0
Kd group	154	122	100	85	70	55	13	2	0

	KdD (n=312)	Kd (n=154)
Median follow-up time, months	16.9	16.3
Progression/Death, n (%)	110 (35%)	68 (44%)
Median PFS, months	NE	15.8
HR (KdD/Kd) (95% CI)	0.63 (0.46-0.85)	
p-value (1-sided)	0.0014	

Usmani et al, ASH 2019; Dimopoulos et al, *Lancet* 2020

IKEMA

Study design: Isa-Kd vs Kd in relapsed multiple myeloma



Sample size calculation: ~300 patients and 159 PFS events to detect 41% risk reduction in hazard rate for PFS with 90% power and one-sided 0.025 significance level

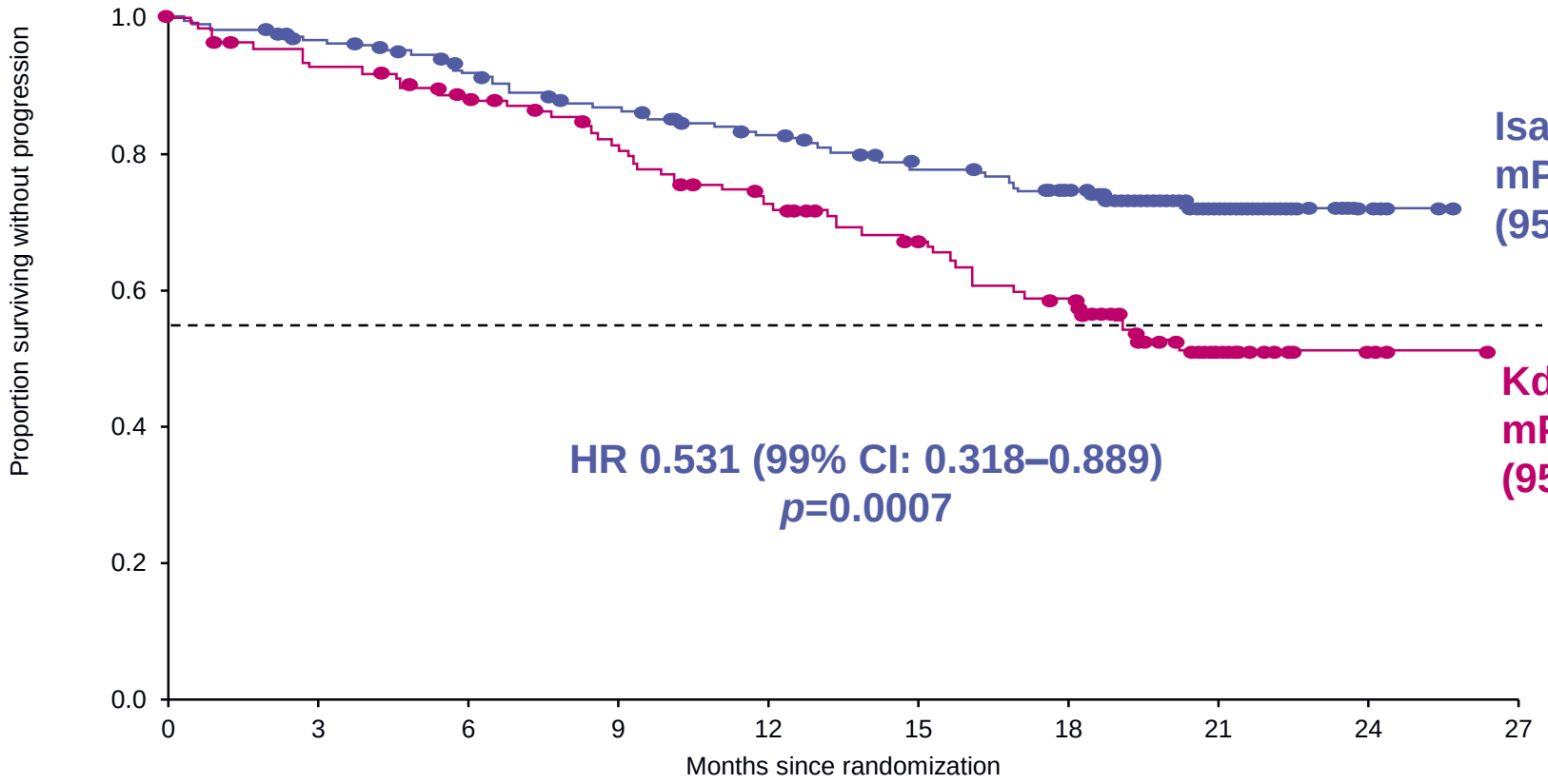
Moreau P, et al. Future Oncol 2020;16:4347–58

IKEMA study: NCT03275285

C, cycle; CR, complete response; D, day; d, dexamethasone; IRC, Independent Review Committee; Isa, isatuximab; K, carfilzomib; MM, multiple myeloma; MRD, minimal residual disease; ms, months; ORR, overall response rate; OS, overall survival; PFS, progression free survival; Q2W, once every 2 weeks; R-ISS, revised international staging system; VGPR, very good partial response

IKEMA

Interim PFS analysis – IRC assessment in ITT population (primary endpoint)



No. at risk										
Isa-Kd	179	164	151	136	124	110	100	36	5	0
Kd	123	108	99	85	72	61	50	19	6	0

One-sided *p* value, level of significance <0.005

Isa-Kd showed improvement in PFS with 47% reduction of risk of progression or death vs Kd

SANOFI GENZYME

CI, confidence interval; d, dexamethasone; HR, hazard ratio; IRC, Independent Review Committee;
Isa, isatuximab; ITT, intent to treat; K, carfilzomib; m, median; NE, not estimable; NR, not reached; PFS, progression-free survival

To recap…

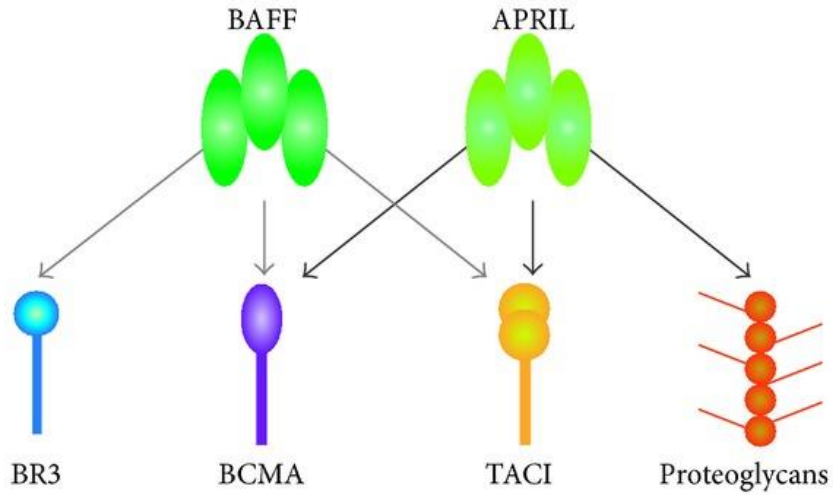
- 3 drugs are better than 2
- Lenalidomide-refractory patients:
  - Daratumumab-pomalidomde-dex
  - Isatuximab-pomalidomide-dex
  - Daratumumab-carfilzomib-dex
  - Isatuximab-carfilzomib-dex

The “IT” girls of MM therapy

- BCMA targeting therapies
  - CAR T cells
  - Bispecific T cell engagers
  - Antibody drug conjugates

BCMA: B cell maturation antigen

- Member of TNFR (TNFRS17)
- Regulate B cell proliferation and survival, maturation to plasma cells
- Expression/ activation associated with myeloma cell growth/ survival
- Exclusively expressed on the surface of plasmablasts and differentiated PCs



Cho et al, *Frontiers in Immunol,* 2018
Tobon et al, *Autoimm Dis,* 2013

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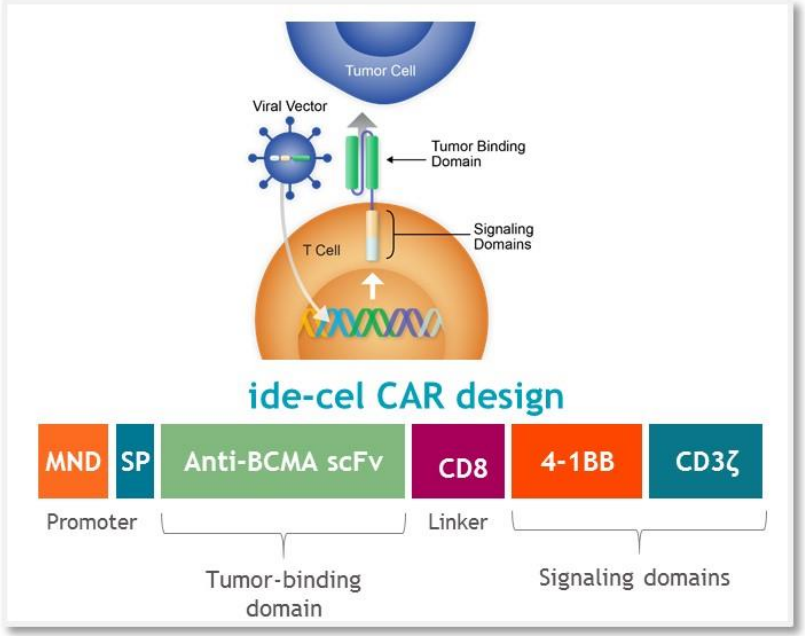
Introduction and Objective

- Outcomes remain poor in triple-class exposed RRMM patients who progress on IMiD® agents, proteasome inhibitors (PIs), and anti-CD38 antibodies, and there is no standard of care
  - Deep and durable responses uncommon[1-3]
  - Median PFS of 3-4 mo; median OS of 9.3 mo[4]
- Ide-cel, a BCMA-directed CAR T cell therapy, showed promising tolerability and efficacy in RRMM patients in the phase I CRB-401 study[5]
  - Evaluated doses of 50–800 × 10^6 CAR+ T cells
  - ORR=85%; CRR=45%; median PFS=11.8 mo; median DOR=10.9 mo
  - Grade ≥3 CRS or neurotoxicity observed in 6% of patients

Objective: To present efficacy and safety data from the pivotal phase II KarMMa trial of ide-cel in RRMM*



Ide-cel CAR T cell Design

- **Autologous** T cells transduced with a lentiviral vector encoding a CAR specific for human BCMA
- Targeting domain: **anti-BCMA**
- Costimulatory domain: **4-1BB**
- T-cell activation domain: **CD3ζ**

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CRR, complete response rate; IMiD, immunomodulatory drug; ORR, overall response rate; PFS, progression-free survival; RRMM, relapsed and refractory multiple myeloma; TM, transmembrane. *Data presented are updated from the protocol-specified primary analysis dataset.

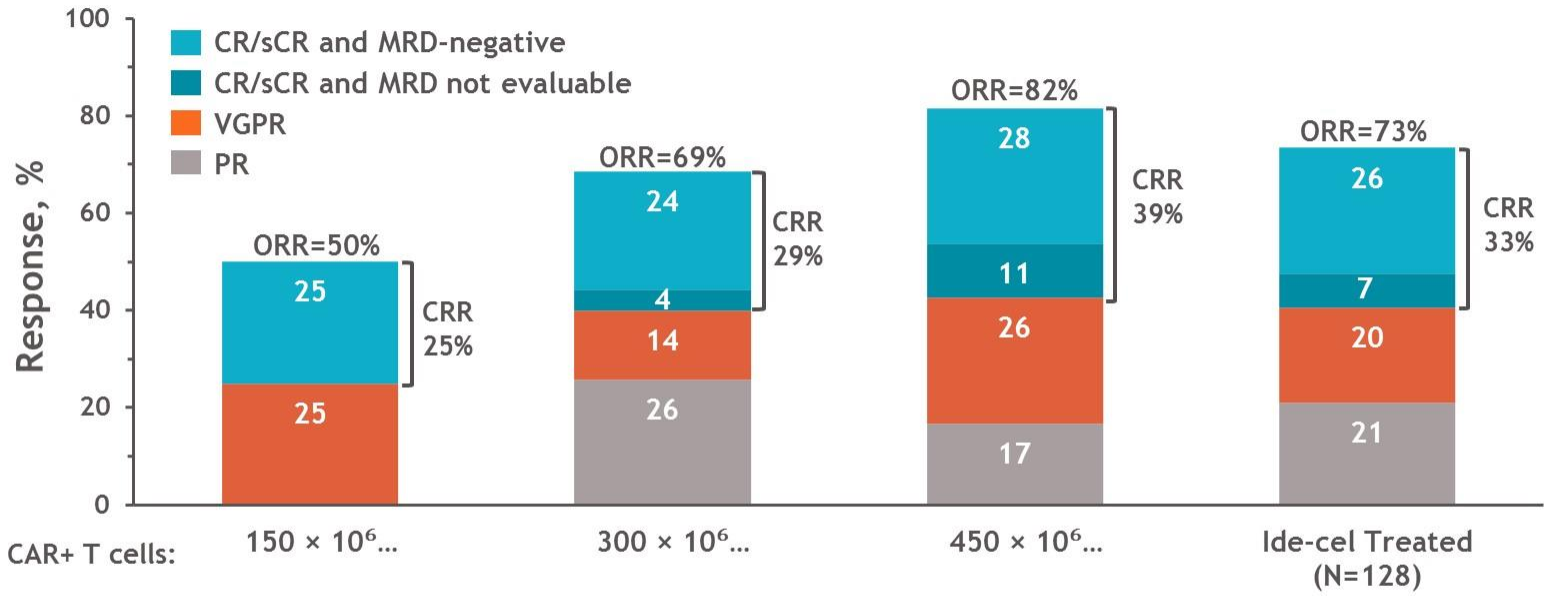
1. Braggio E, et al. *Cancer Cell* 2015;28:678-.e1. 2. Rasche L, et al. *Cancer Treat Rev* 2017;55:190-9. 3. Nijhof IS, et al. *Drugs* 2018;78:19-37. 4. Gandhi UH. *Leukemia.* 2019;33:2266-75. 5. Raje NS, et al. *N Engl J Med.* 2019;380:1726-1737.

Munshi et al, ASCO 2020

Best Overall Response

Median # prior regimens: 6

CRS: 84%
Neurotox: 18%

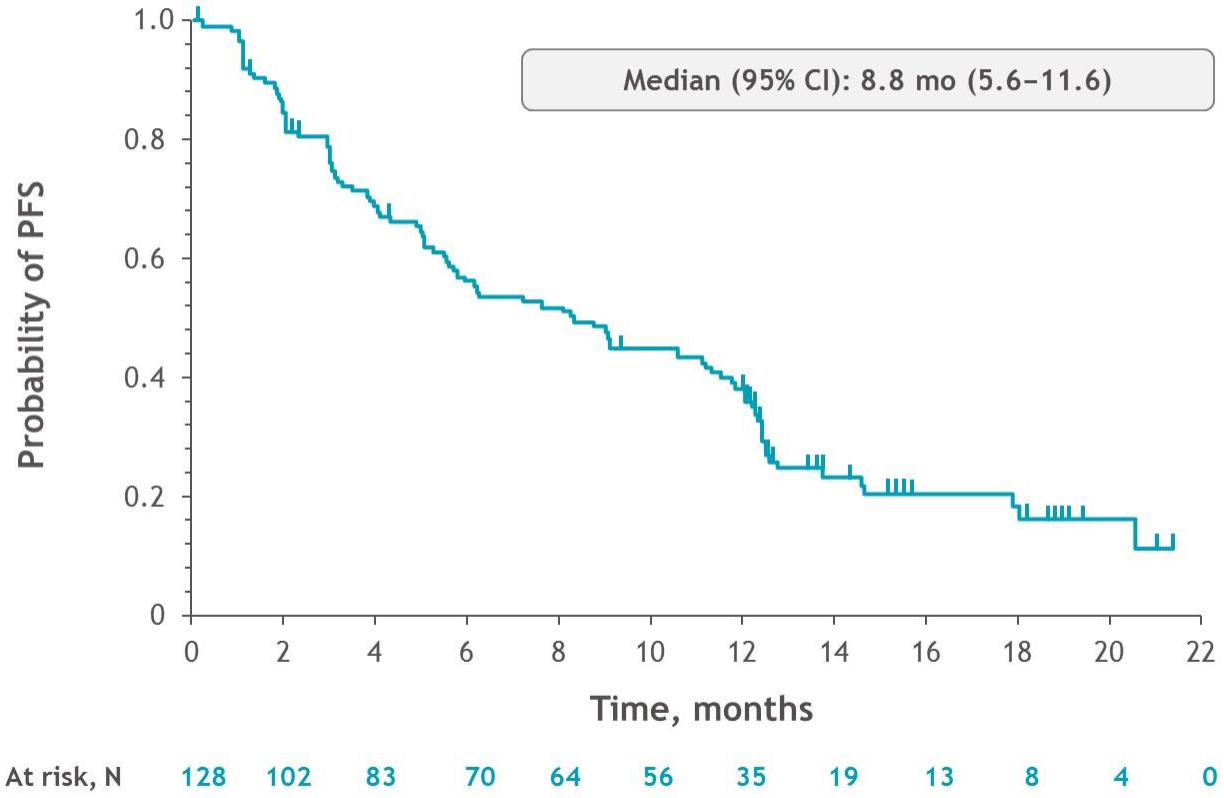


- Primary (ORR >50%) and key secondary (CRR >10%) endpoints met in the ide-cel treated population
  - *ORR of 73% (95% CI, 65.8–81.1; P<0.0001*)*
  - *CRR (CR/sCR) of 33% (95% CI, 24.7–40.9; P<0.0001)*
- Median time to first response of 1.0 mo (range, 0.5–8.8); median time to CR of 2.8 mo (range, 1.0–11.8)
- Median follow-up of 13.3 mo across target dose levels

Data cutoff: 14 Jan 2020. MRD-negative defined as $<10^{-5}$ nucleated cells by next generation sequencing. Only MRD values within 3 mo of achieving CR/sCR until progression/death (exclusive) were considered.
Values may not add up due to rounding.
CR/sCR, complete response/stringent CR; CRR, CR rate; MRD, minimal residual disease; ORR, overall response rate (≥PR); PR, partial response; VGPR, very good PR. **P* value at the primary data cutoff with same ORR and 95% CI.

Munshi et al, ASCO 2020

Progression-Free Survival

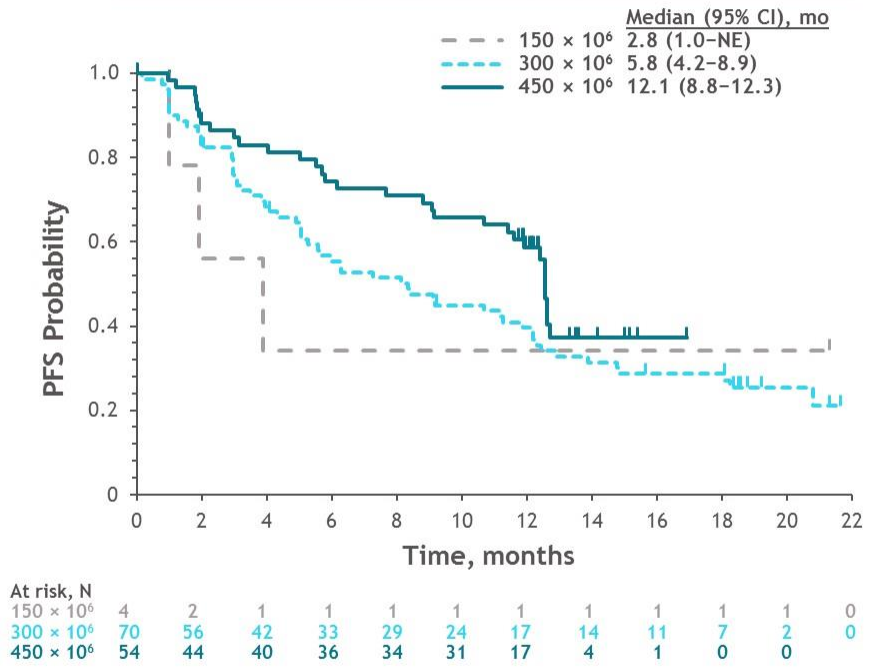


Data cutoff: 14 Jan 2020. PFS, progression-free survival.

Munshi et al, ASCO 2020

Progression-Free Survival

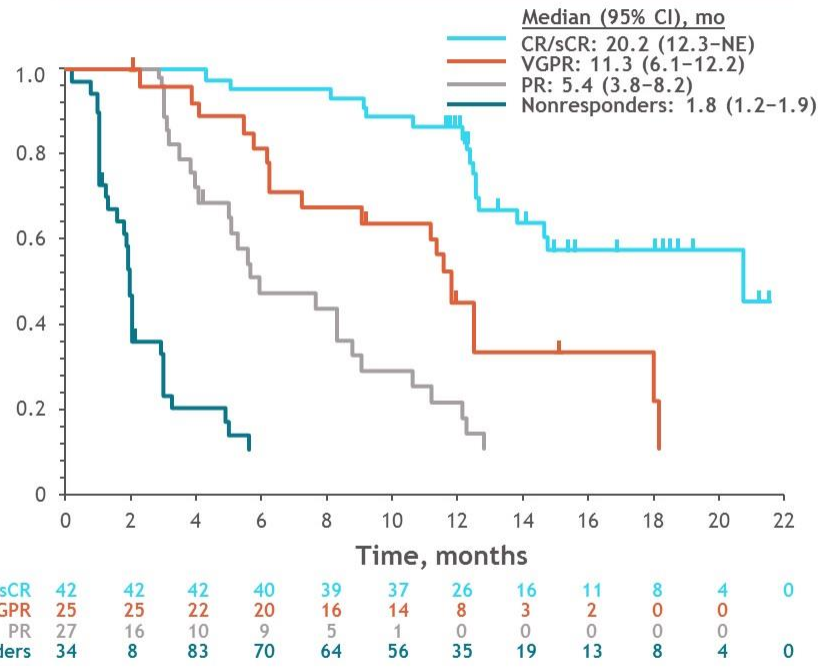
PFS by Target Dose



At risk, N												
150 × 10⁶	4	2	1	1	1	1	1	1	1	1	1	0
300 × 10⁶	70	56	42	33	29	24	17	14	11	7	2	0
450 × 10⁶	54	44	40	36	34	31	17	4	1	0	0	

- PFS increased with higher target dose; median PFS was 12 mo at 450 × 10^6 CAR+ T cells

PFS by Best Response



CR/sCR	42	42	42	40	39	37	26	16	11	8	4	0
VGPR	25	25	22	20	16	14	8	3	2	0	0	
PR	27	16	10	9	5	1	0	0	0	0	0	
Nonresponders	34	8	83	70	64	56	35	19	13	8	4	0

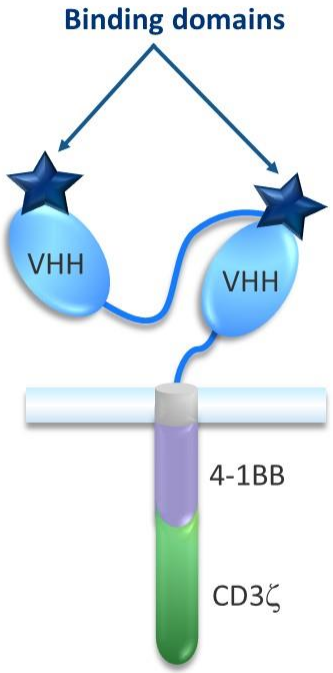
- PFS increased by depth of response; median PFS was 20 mo in patients with CR/sCR

Data cutoff: 14 Jan 2020. NE, not estimable; PFS, progression-free survival.

Munshi et al, ASCO 2020

JNJ-4528: BCMA-targeted CAR-T Cell Therapy

- **JNJ-68284528 (JNJ-4528) is a structurally differentiated chimeric antigen receptor T (CAR-T) cell therapy**
  - Contains a CD3ζ signaling domain and 4-1BB costimulatory domain
  - 2 BCMA-targeting single chain antibody designed to confer avidity
  - Identical to the CAR construct used in the LEGEND-2 study
- **Deep and durable responses observed in patients with R/R MM**
  - LEGEND-2 (N = 57): mPFS of 20 mo and mOS of 36 mo at median 25-mo follow-up[1]
    - CRS events were mostly grade 1 – 2; one grade 1 neurotoxic event



JNJ-4528 CAR

[1]Wang et al. *Blood* 2019;134(Suppl_1):579 (oral presentation); BCMA=B-cell maturation antigen; CRS-cytokine release syndrome; mPFS=median progression-free survival; MM=multiple myeloma; mOS=median overall survival; ORR=overall response rate; R/R=relapsed/refractory; VHH=single variable domain on a heavy chain

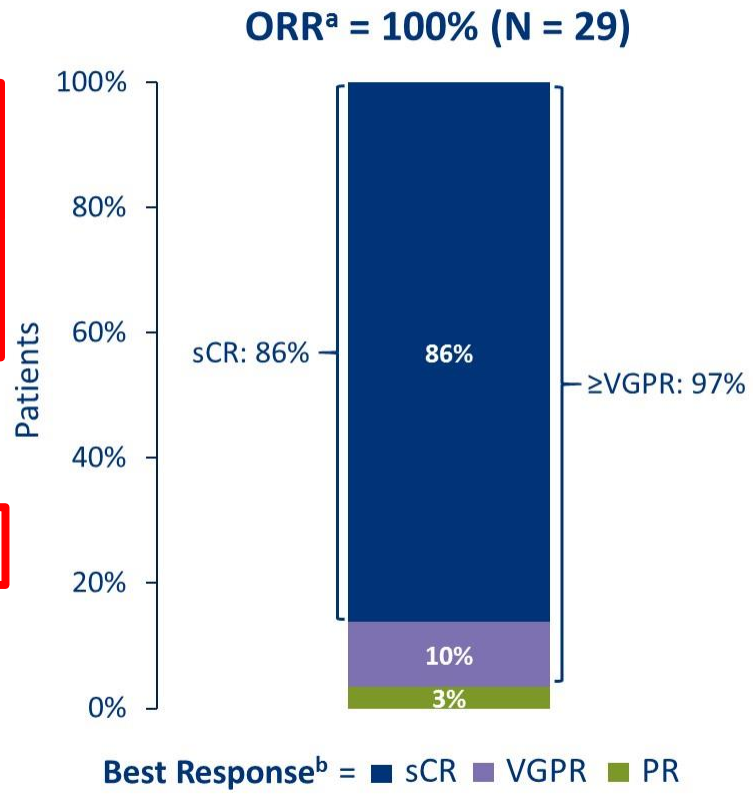
Berdeja et al, ASCO 2020

CARTITUDE-1: Overall Response Rate

Median # prior regimens: 6

CRS: 93%
Neurotox: 10%

9 mo PFS 86%



- 25 of 29 (86%) patients achieved sCR
- ORR and depth of response were independent of BCMA expression on myeloma cells at baseline
- Median time to first response = 1 mo (1 – 3)
- Median time to CR = 3 mo (1 – 13)

[a]PR or better; Independent Review Committee-assessed, [b]No patient had complete response, stable disease, or progressive disease as best response. CR=complete response; ORR=overall response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

Berdeja et al, ASCO 2020

BCMA CAR-T Cells ASCO 2020

Safety

	KarMMa	EVOLVE	CARTITUDE-1
↓ ANC ≥G3, %	89	90	100
↓ Plts ≥G3, %	52	47	69
CRS: all, ≤G3, %	84, 6	89, 3	93, 7
Med. Time to CRS, duration, days	1 (1-12) 5 (1-63)	2 (1-4) 4 (1—10)	7 (2-12) 4 (2-64)
ICANS: all, ≤G3, %	17, 3	13, 3	10, 3
HLH/MAS, %	--	5	? 7 (lfts)
Infections: all, ≥G3 %	69, --	40, 13	--, 19
Toci / steroid / anakinra use, %	52/15/0	76/52/23	79/21/21

Efficacy

	KarMMa (n = 128)	EVOLVE (n = 62)	CARTITUDE-1 (n = 29)
ORR, %	73 (66-82)	92	100
sCR/CR, %	33	36	86
MRD neg ≥10^{-5}, % evaluable	94	84	81
PFS/DoR, months	8.8/10.7	NR	NR
Screened Apheresed Treated	150 140 128	--	35 35 29

Munshi NC et al. ASCO 2020. Abstract 8503; Mailankody S et al. ASCO 2020. Abstract 8504; Berdeja JG et al. ASCO 2020. Abstract 8505.

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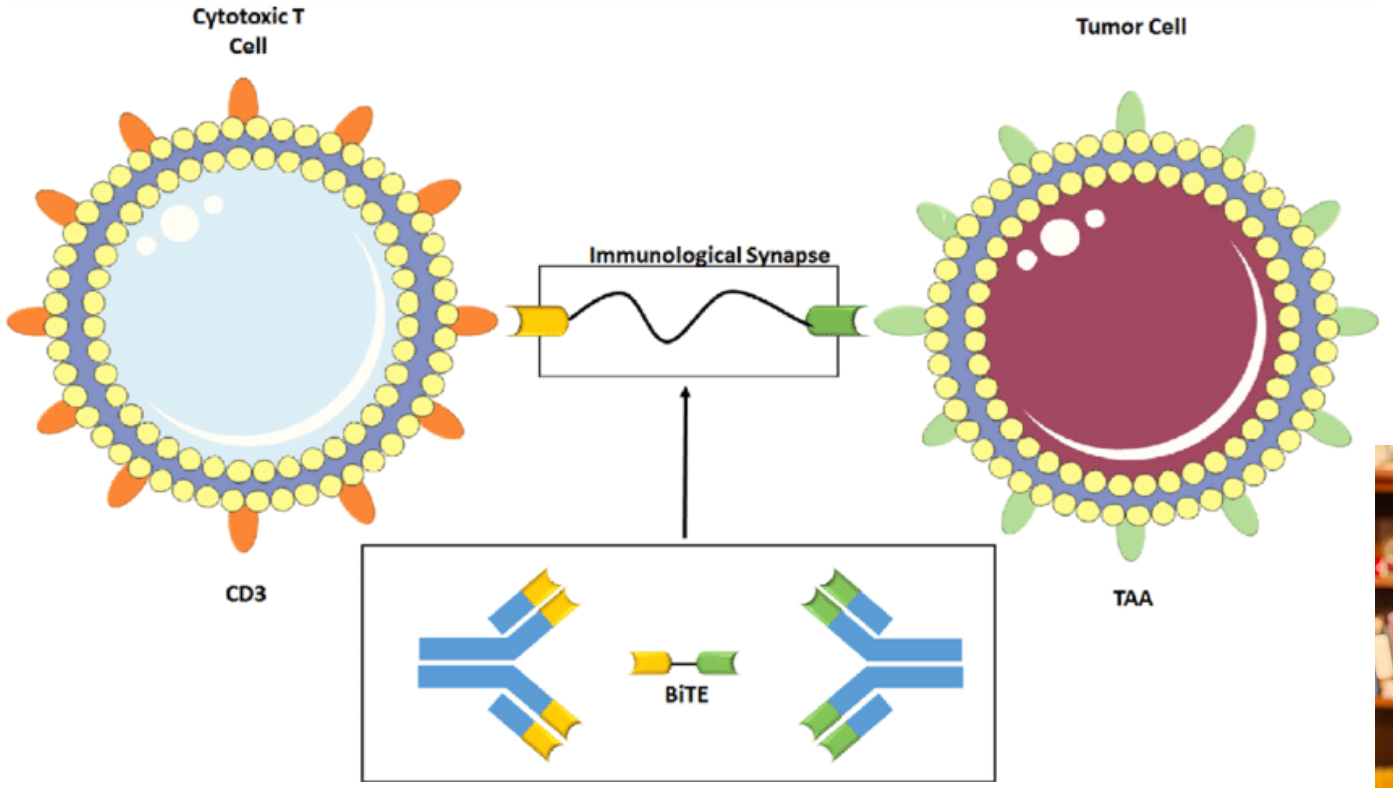
Bispecific T cell engagers



"Hello, I am Sima from Mumbai…"

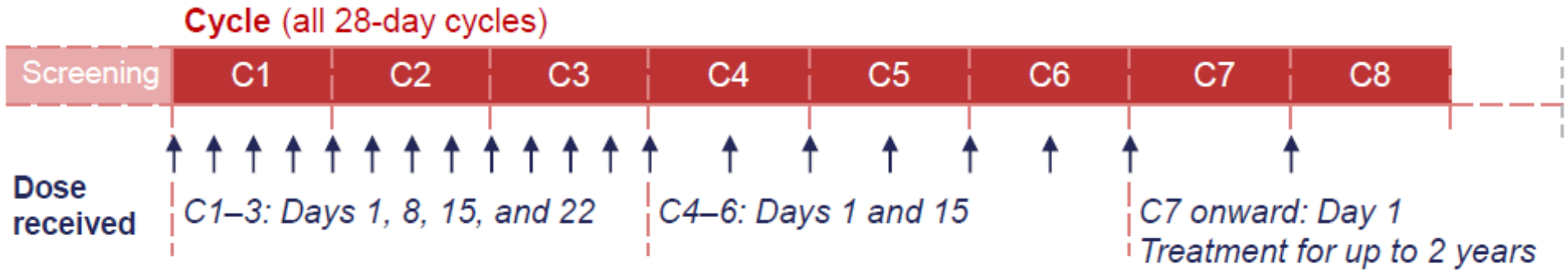
UCSF

CC-93269-MM-001 PHASE 1 TRIAL (NCT03486067): STUDY DESIGN

Key Eligibility Criteria

- RRMM after ≥ 3 prior regimens
- Progressive disease within 60 days of last regimen
- No prior BCMA-directed therapy

Dose Schedule



All doses administered via IV over 2 hours

Part A: Dose Escalation

- Stage 1: Fixed doses
- Stage 2: Step-up in dose on C1D8

Part B: Cohort Expansion

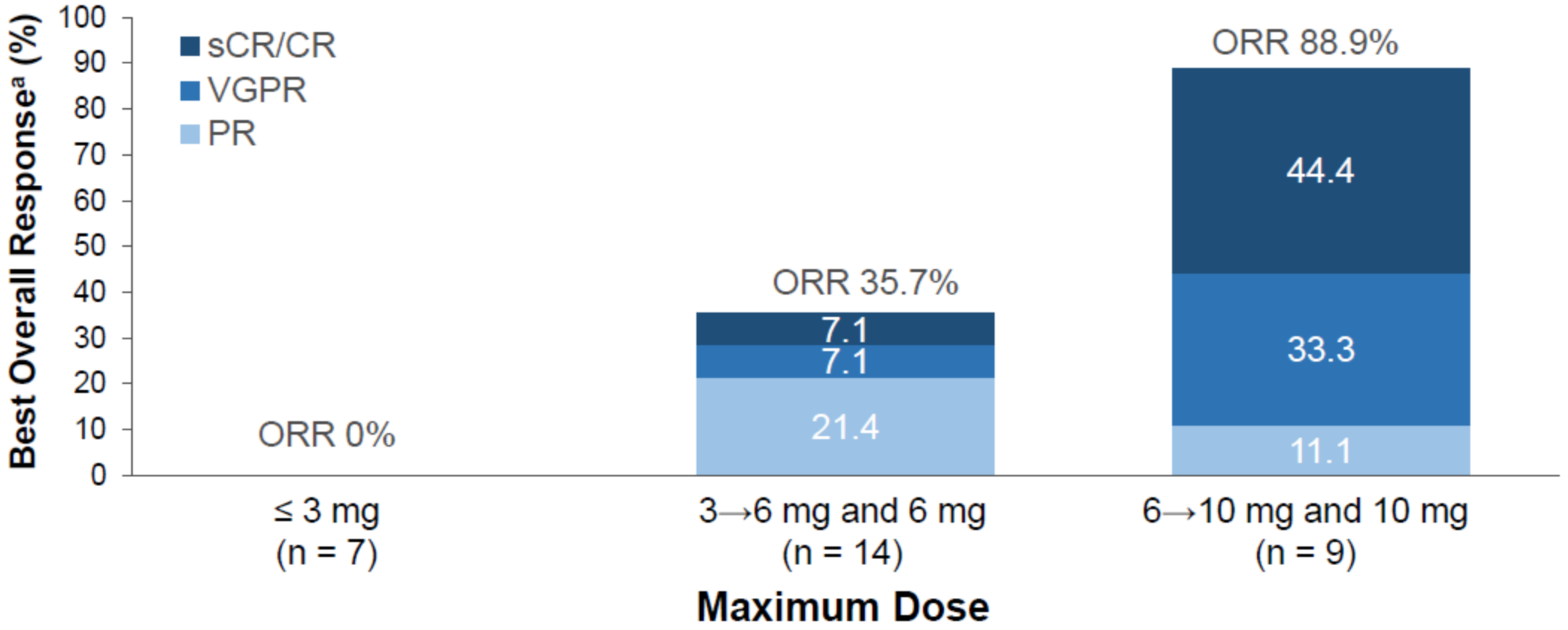
Endpoints

Primary: Safety including DLTs, AEs, NTD, and MTD
Secondary: Preliminary efficacy including MRD, PK, ADA, and PD endpoints

ADA, anti-drug antibody; AE, adverse event; C, Cycle; D, Day; DLT, dose-limiting toxicity; IV, intravenous; MRD, minimal residual disease; MTD, maximum tolerated dose; NTD, non-tolerated dose; PD, pharmacodynamics; RRMM relapsed/refractory multiple myeloma.

CC-93269 PRELIMINARY EFFICACY

Median # prior regimens: 5



- In all patients (N = 30), the ORR was 43.3% with a sCR/CR of 16.7%
- Among patients receiving 10 mg (n = 9), the ORR was 88.9% with a sCR/CR of 44.4%

CRS: 77%

Data as of October 28, 2019.
[a] Response as assessed by the investigator.
CR, complete response; ORR, overall response rate (PR or better); PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Teclistamab: Phase 1 Study Design

Key Objectives

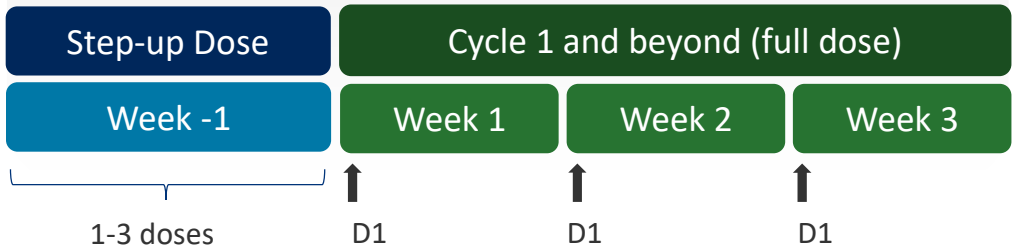
- Part 1: Identify RP2D
- Part 2: Safety and tolerability
- Antitumor activity, PK, PD

Key Eligibility Criteria

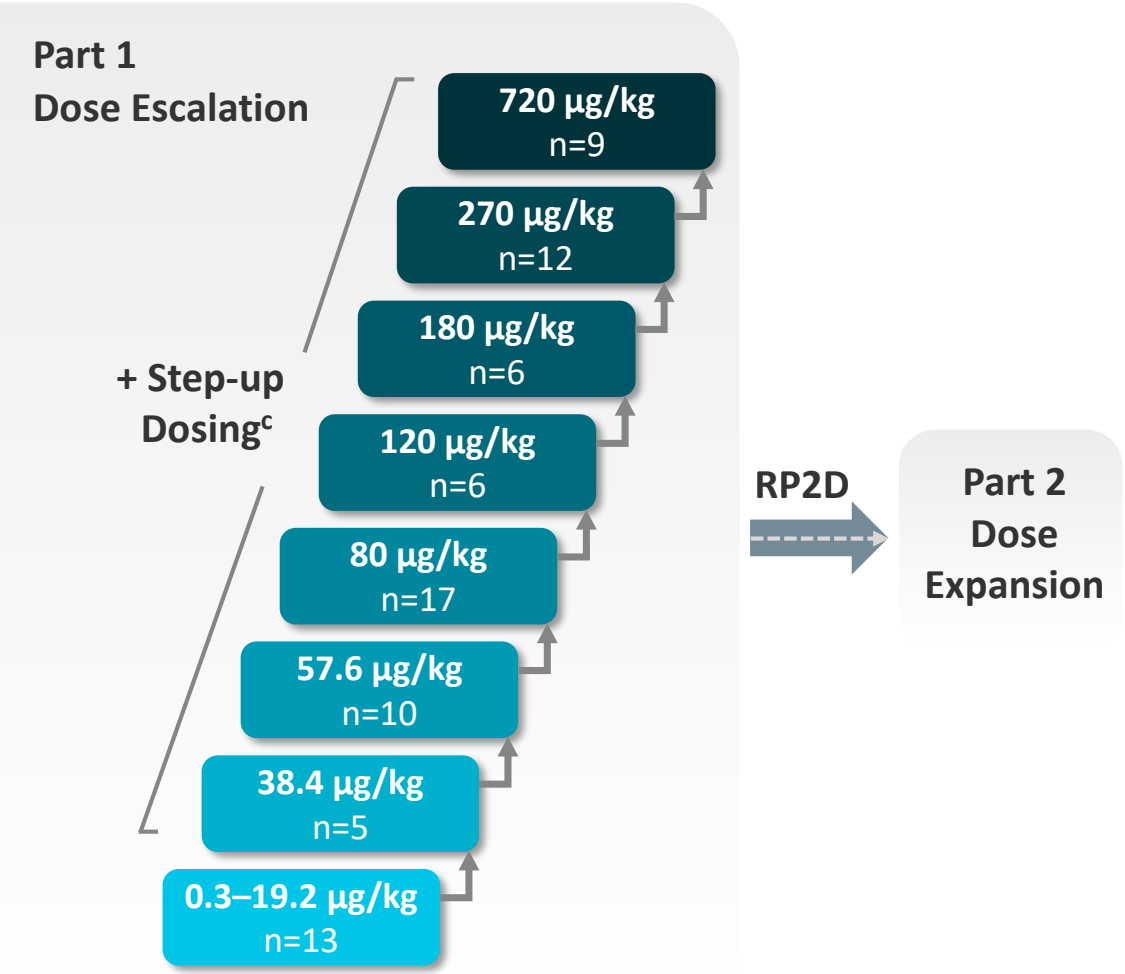
- Measurable MM
- RR or intolerant to established MM therapies
- Hb ≥8 g/dL, platelets[a] ≥75x10^9/L, ANC ≥1.0x10^9/L
- No prior BCMA-targeted therapy

Intravenous Dosing

- Initial Q2W dosing switched to weekly ± step-up dosing
- Pre-medications[b] limited to step-up doses and 1st full dose



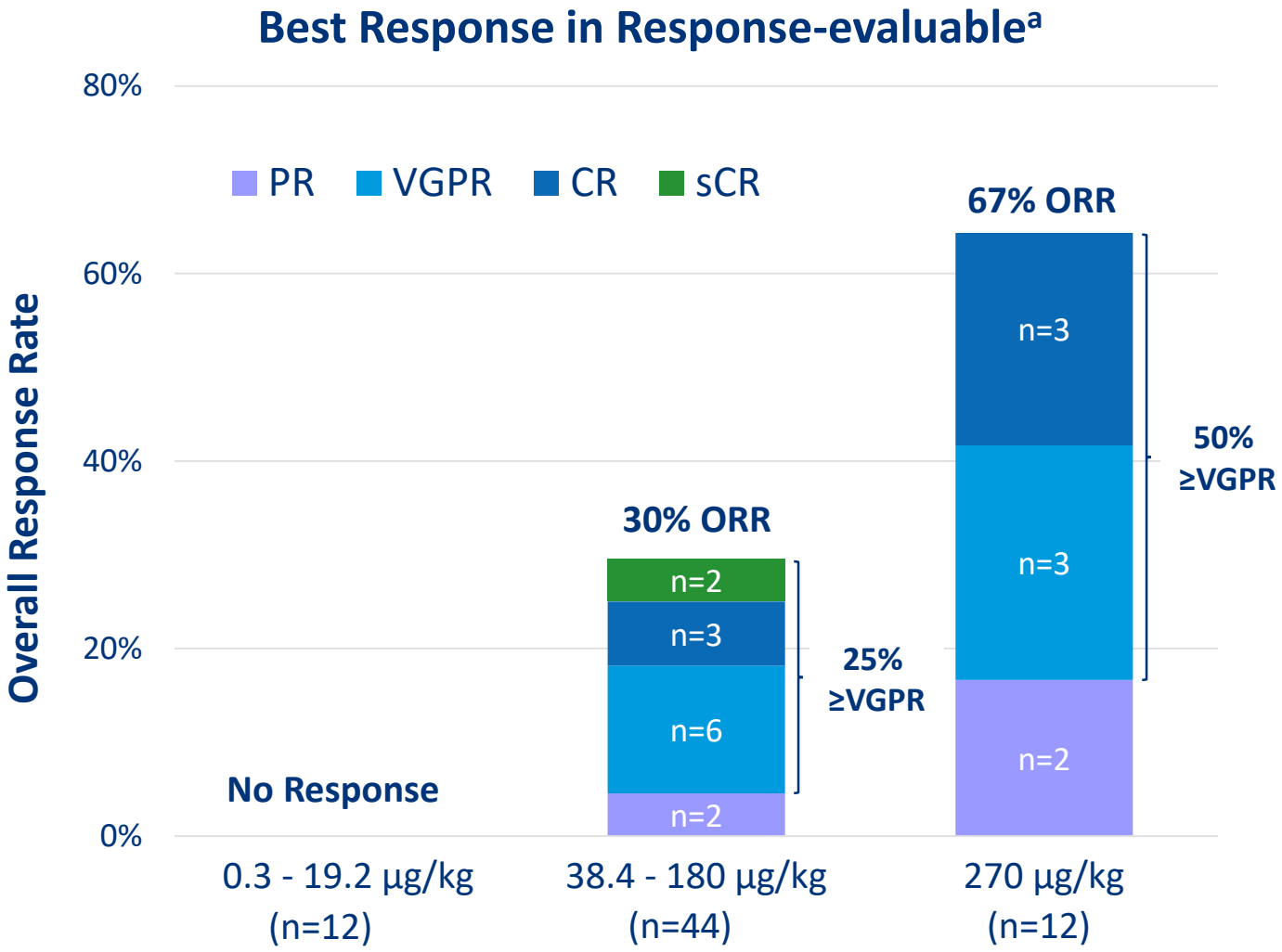
- **Results from Part 1 intravenous dose escalation are presented**



Data cutoff: 30 Apr 2020. [a]≥50x10^9/L for patients with ≥50% bone marrow plasma cells, [b]Glucocorticoid, antihistamine, antipyretic, H_2-antagonist, and antiemetic, [c]1-3 step-up doses given within 1 week before full dose.
ANC=absolute neutrophil count; Hb=hemoglobin; PD=pharmacodynamics; PK=pharmacokinetics; Q2W=every 2 weeks; RP2D=recommended phase 2 dose

56th ASCO Annual Meeting 2020, Usmani SZ, et al. Abstract #100

Teclistamab: Overall Response Rate



CRS: 56%
Neurotox: 8%

Median # prior regimens: 6

- Efficacy data at 720 µg/kg dose are not mature
- At the 270 µg/kg dose, 7/8 responders were triple-class refractory; 5/8 were penta-drug refractory
- 4/5 evaluable-patients[b] were MRD-negative at 10^{-6}; 2 had MRD-negative CR
- 2/2 evaluable patients maintained MRD-negativity for 5 months (VGPR) and 14 months (CR)

[a]Response-evaluable patients received at least one study treatment with at least 1-month follow-up or at least one response evaluation, [b]MRD-evaluable patients have suspected CR and identified baseline clone for assessment.
CR=complete response; MRD=minimal residual disease; ORR=overall response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

56th ASCO Annual Meeting 2020, Usmani SZ, et al. Abstract #100

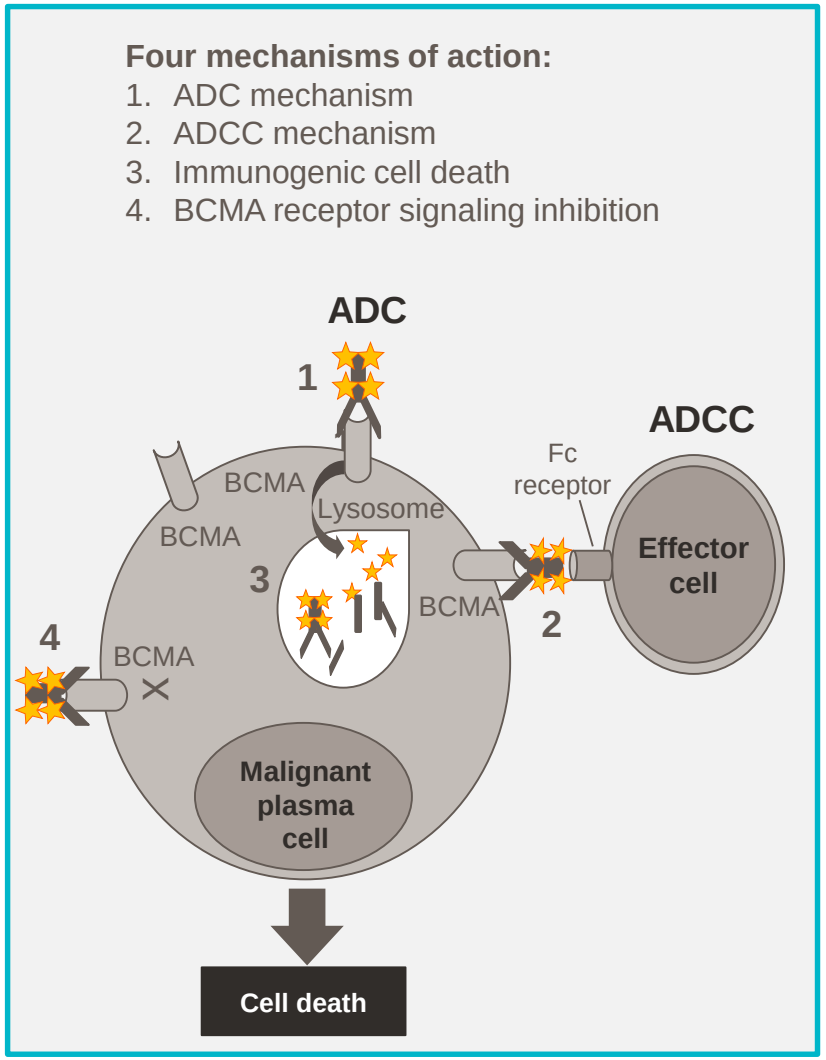
Belantamab mafodotin

- BCMA: expressed on differentiated B cells; requisite for long-lived plasma cells' survival
- **BCMA is broadly expressed on malignant plasma cells**
- **GSK2857916:** humanized, afucosylated IgG1 **anti-BCMA antibody;** neutralization of soluble BCMA
  - Preclinical studies demonstrate its selective and potent activity[1]

GSK2857916

Cytotoxic agent	– MMAF (non-cell permeable, highly potent auristatin
Afucosylation	– Enhanced ADCC
Linker	– Stable in circulation

FDA approved 8/5/20



[1]Tai YT, et al. Blood 2014;123(20):3128-38.

ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; BCMA, B-cell maturation antigen; IgG, immunoglobulin G; MMAF, monomethyl auristatin-F

DREAMM-2

Patient Characteristics[1,2]

DREAMM-2 overall population: refractory to proteasome inhibitor, immunomodulatory agent, and exposed to an anti-CD38 treatment[1,2] belantamab mafodotin 2.5mg/kg (n=97)	
Age, median (IQR), years	65.0 (60-70)
ECOG PS 2, n (%)	16 (17)
ISS stage, n (%)	
I	21 (22)*
II	33 (34)*
III	42 (43)*
Unknown	1 (1)*
High-risk cytogenetics (IMWG 2014 defined), n (%)	**41 (42)**
Median number of prior lines of therapy	**7 (3-21)**
>4 lines, n (%)	81 (84)
Refractory to daratumumab, n (%)	**97 (100)**
Refractory to prior therapies‡	
Proteasome inhibitor	
Bortezomib	74 (76)
Carfilzomib	63 (65)
Immunomodulatory drug	
Lenalidomide	87 (90)
Pomalidomide	84 (87)
Anti-CD38 monoclonal antibody	
Daratumumab	97 (100)
Isatuximab	3 (3)

- Patients studied in the DREAMM-2 trial were refractory to prior immunomodulatory agents, PIs, and refractory and/or intolerant to an anti-CD38 antibody.
- In the 2.5 mg/kg cohort, 100% of the patients were refractory to an anti-CD38 antibody.

*ISS stage at screening

‡Based on data available at the time of database lock; however, all patients were refractory to a proteasome inhibitor, immunomodulatory drug, and an anti-CD38 monoclonal antibody as per eligibility criteria.

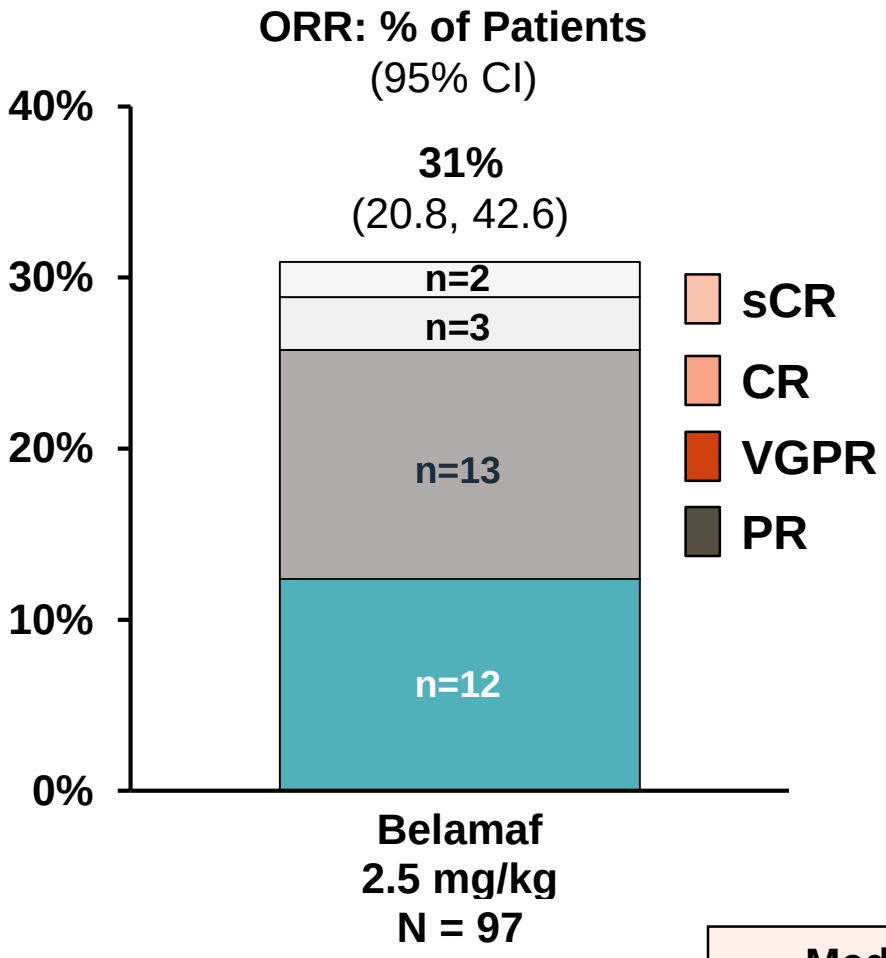
PI = proteasome inhibitor

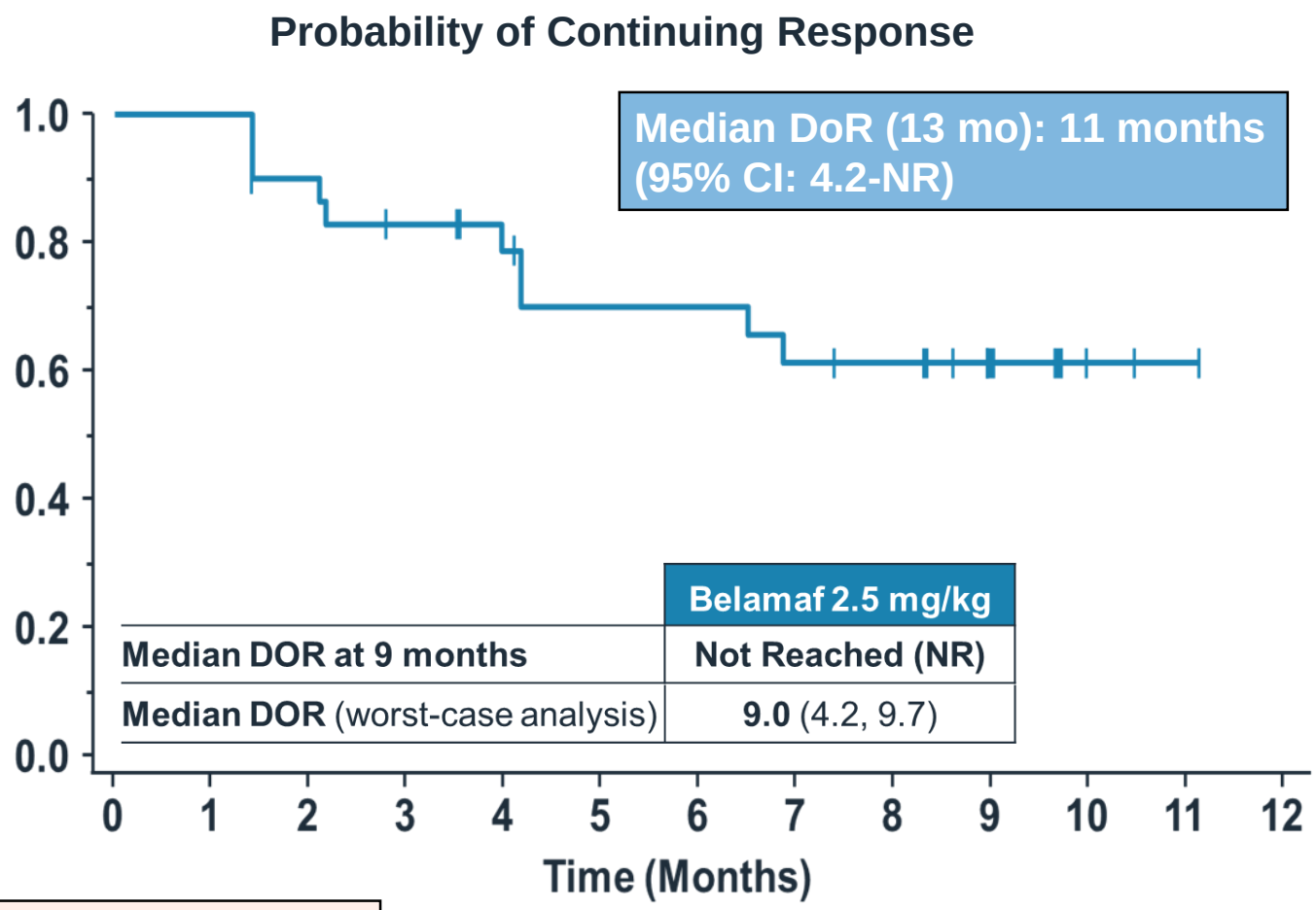
ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; ISS, International Staging System.

1. Lonial S et al. Lancet Oncol. 2020;21:207-221.
2. Data on File. Philadelphia, PA: GlaxoSmithKline, Inc; 2019.

DREAMM-2

Belantamab Mafodotin Demonstrated Deep and Durable Responses

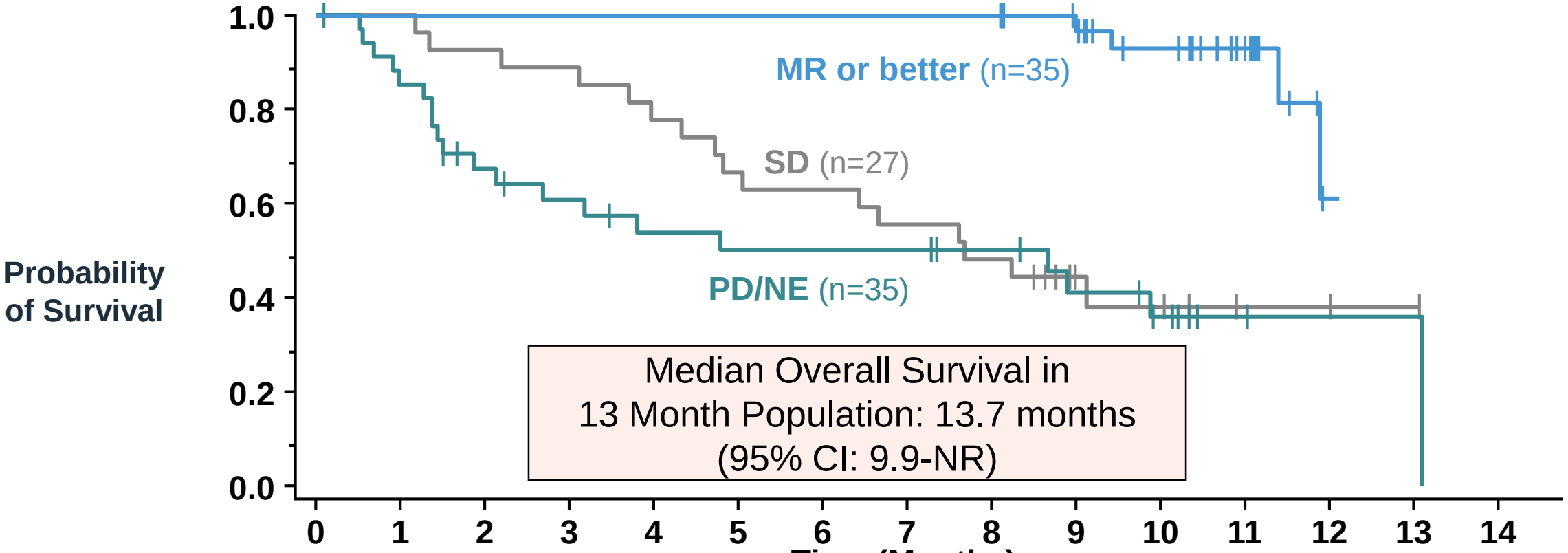




Median PFS: 2.8 months
(95% CI: 1.6-3.6)

Based on 9-month update

DREAMM-2: Overall Survival by Response in Patients Receiving Belantamab Mafodotin 2.5 mg/kg



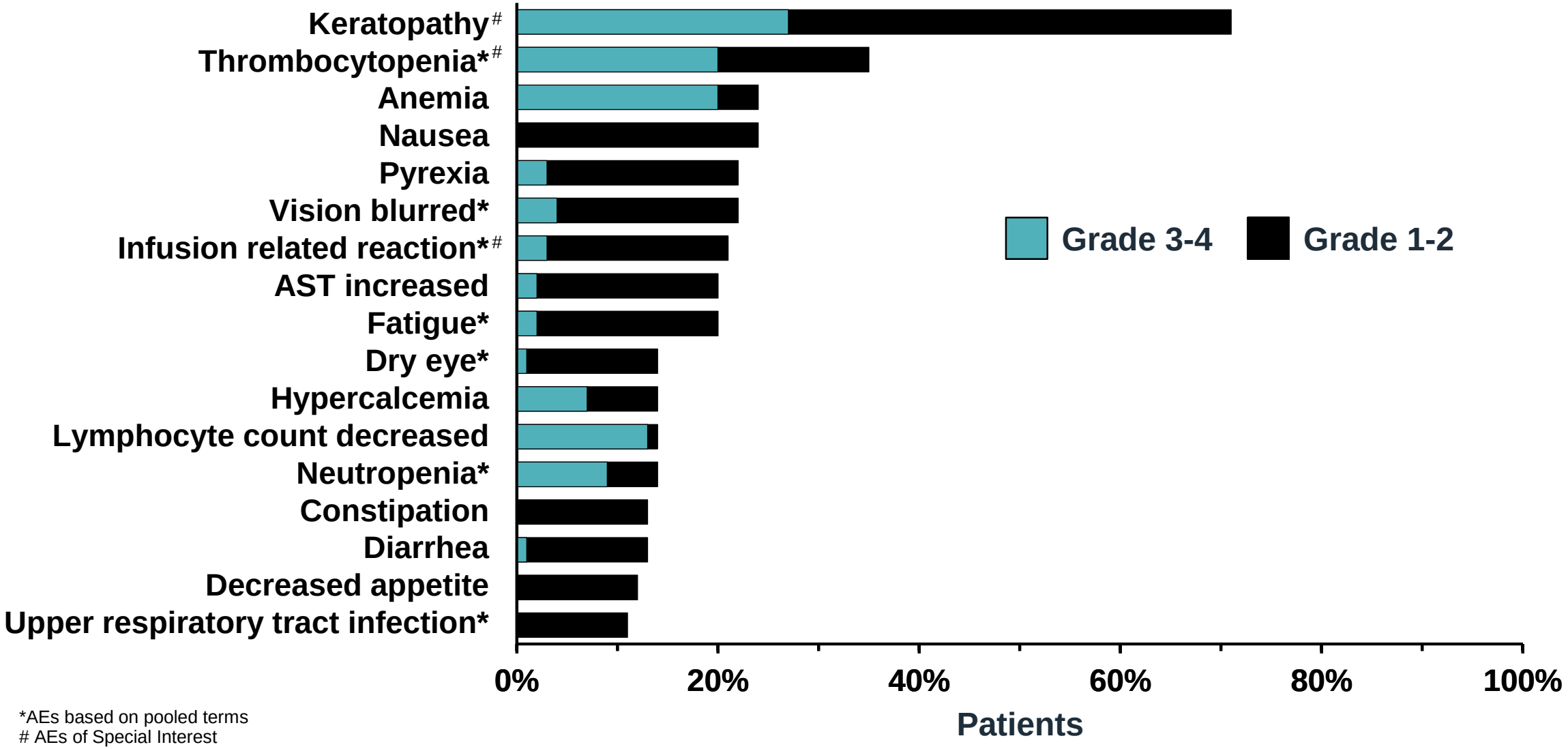
Number at Risk															
ORR + MR	35	35	35	35	35	35	35	35	35	31	24	15	1	0	
SD	27	27	25	24	21	18	17	15	13	8	6	2	2	1	0
PD / NE	35	29	21	18	15	14	14	14	12	9	6	2	1	1	0

MR = minimal response; NE = not evaluable; ORR = overall response rate; PD = progressive disease; SD = stable disease
Based on 9-month update. Data on File

The DREAMM-2 Study

DREAMM-2

Most Common AEs by CTCAE Grade for Belantamab Mafodotin 2.5 mg/kg



*AEs based on pooled terms
AEs of Special Interest
Any grade in ≥ 10% of patients

The DREAMM-2 Study

Comparing options

	CAR T	Bispecifics	ADCs
Treatment logistics	Specialized center, need to wait for production	TBA, likely community-friendly, off-the shelf Need for long-acting	community-friendly, off-the shelf
Length of treatment	~2 months	??	Possibly limited cycles
Toxicities	CRS, neurotoxicity, cytopenias	CRS, pneumonia	Corneal, thrombocytopenia
Cost	? $400K	? But have to consider length of treatment	$24K/month

Conclusions

- No one way to treat relapsed myeloma
- Novel agents moving forward
- BCMA- targeting agents poised to change the landscape of triple-class refractory disease

THANK YOU!

@ninashah33

#myelennial

UCSF

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INTERNATIONAL **MYELOMA** FOUNDATION

Improving Lives. **Finding the Cure.**

“Navigating the Journey”

Kimberly Noonan, RN, ANP, AOCN

Dana-Farber Cancer Institute

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REGIONAL COMMUNITY WORKSHOP

Be the Commander of Your Galactic Journey: Navigating the Journey

Presenter: **Kim Noonan** DNP, RN, ANP, AOCN
Dana-Farber Cancer Institute
kimberly_noonan@dfci.harvard.edu

Southwestern USA Regional Community Workshop

November 14, 2020

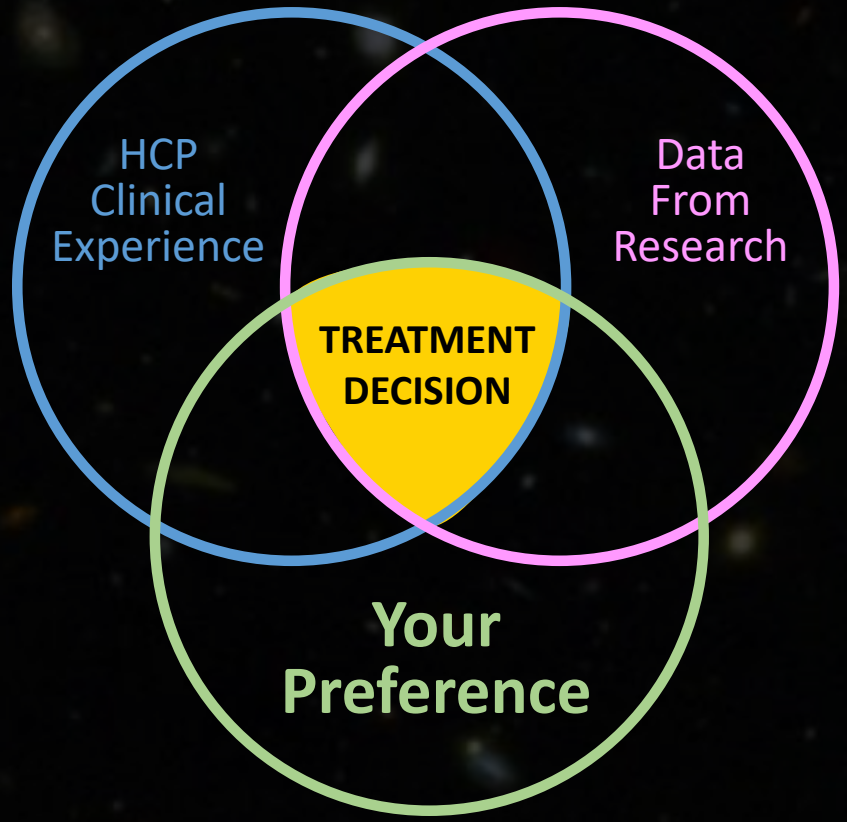
You are in the Commander's Chair

Be an Empowered Patient
"Scotty, We Need More Power!"

- Participate in decisions
- Ask for time to consider options
  (if needed/appropriate)
- Understand options
  - Use reliable sources of information
  - Use caution considering stories of personal experiences
- Create a dialogue
- Express your goals/values/preferences
- Arrive at a treatment decision together

Explore Treatment Options & Plan Your Course

Drug class	Myeloma therapies	Common combinations
Proteosome inhibitor	Bortezomib (SQ)	VRD, Vd
	Carfilzomib	KRd, Kd, K
	Ixazomib	IxRd
Immuno-modulatory agent	Pomalidomide	Pd, DPd, EPd
	Lenalidomide	VRD, Rd
	Thalidomide	Dara + VTd
Monoclonal antibody	Daratumumab	DRd, DVd, DPd, D-VMP
	Elotuzumab	ERd, EPd
	Isatuximab-irfc	IsaPd
Antibody-drug conjugate	Belantamab mafadotin	Bela montherapy
Nuclear export inhibitor	Selinexor	Sel + d, Sel + Vd
Anthracycline	Liposomal doxorubicin	BRd, BVd
Alkylating agents	Cyclophosphamide	PCd, VTD-PACE
	Melphalan	MVP, MPT
HDACi	Panobinostat	Panobinostat + Vd
Many	Clinical trials are always an option	



Philippe Moreau. ASH 2015.

Bela = belantamab C = cyclophosphamide; D = daratumumab; d = dexamethasone; E = elotuzumab; HDACi = histone deacytlase inhibitor; Isa = Isatuximab; Ix = ixazomib; K = carfilzomib; P = pomalidomide; R = lenalidomide; Sel = Selinexor; SQ = subcutaneous; V = bortezomib

Faiman B, et al. *J Adv Pract Oncol.* 2016;2016:7(suppl 1):17-29. Philippe Moreau. ASH 2015; Prescribing information.

Communicate Symptoms with Your Team

Poorly managed symptoms can lead to...

- Anxiety
- Depression
- Social isolation
- Missed doses
- Reduced treatment efficacy
- Reduced quality of life

Discuss how you feel with your team...

- Keep a symptom diary; discuss with team
- Many options but your team cannot help if they don’t know
- Express your priorities
  - Fatigue is common concern but making the right treatment decision is higher priority for most

Faiman, B. *CJON.* 2017, 21(5)suppl 3-6. Faiman, B. et al 2017. Patient Reported Symptoms, Concerns and Provider Intervention in Patients with Multiple Myeloma

All Crew Members are Needed for a Successful Journey

Subspecialists

General Hem/Onc

Primary Care Provider (PCP)

You and Your Caregiver(s)

Myeloma Specialist

Family/Support Network

Allied Health Staff

- You and your caregiver are the center
- Understand the different roles of your health care team
- Understand how they can help you

Major Tom to Ground Control… Communicating Effectively with Your Crew

Navigating the Journey

Prepare for Your Away Mission	Achieve Your Appointment	Navigate Home
• Write down your questions and concerns • Bring current medications and supplements or a list • Any medical or life changes since your last visit? • Current symptoms - how have they changed?	• Speak up! • Ask your most important questions first • Understand your treatment plan and next steps • Have a list of who to contact and when • Bring a Caregiver for another “set of ears”	• Communicate with other members of your health care crew (pharmacist, others) • Take your medications as directed • Follow up with members of your heath care crew

Caregivers Are An Essential Part of the Crew

- Myeloma usually treated as outpatient
- Myeloma patients need caregiver support
  - Direct health-related
  - Care coordination/life management
  - Emotional support
- Caregivers can be formal or informal (family, friends, neighbors, church members, etc)
- Caregiving duties may be shared across multiple individuals
- Caregiver stress is common

Kurtin S, et al. *Clin J Oncol Nurs*. 2013;17(6;suppl):25-32.

Don’t Let Inertia Take Over! Keep Moving and Adopt a Healthy lifestyle

Navigating the Journey

Managing stress

Rest, relaxation, sleep hygiene

Maintain a healthy weight, eat nutritiously

Activity / exercise / prevent falls, injury

Stop smoking

Sexual health / intimacy

Mental health / social engagement

Complementary or integrative therapy

Have a PCP for general check ups, preventative care, vaccinations

Skin cancer screening, eye exam, dental

Fueling Up When You're Feeling Well

Navigating the Journey

- ✓ Maintain healthy body weight
- ✓ Eat variety of foods, high in vegetables, fruits, whole grains, and lean protein
- ✓ Limit foods & beverages high in fat and added sugars
- ✓ Incorporate sources of healthy fats: walnuts, canola oil, flaxseed
- ✓ Moderate alcohol consumption
- ✓ Don't use supplements to protect against cancer or to replace a healthy diet

Escape Earth's Gravitational Field - Maintain Strong Bones and Muscles

Navigating the Journey

Benefits of Exercise:

- Positively impacts both mental and physical health
- May reduce pain, fatigue and neuropathy
- Builds a stronger immune system

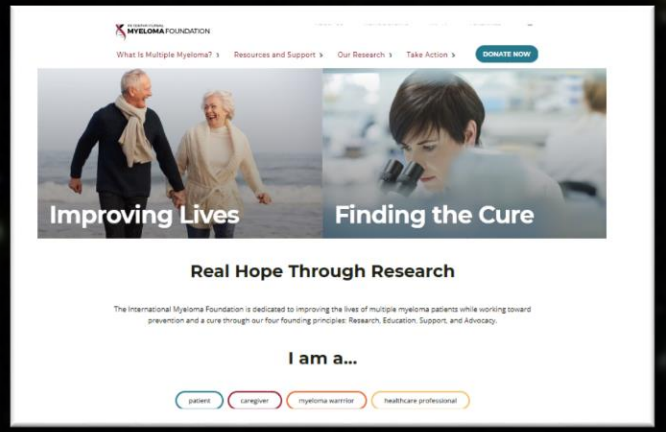
So go for a walk!

…and talk to your doctor before beginning an exercise routine

Knowledge is Power
IMF has many resources to help you learn more

Navigating the Journey

Download or order at myeloma.org



Website: http://myeloma.org

IMF TV Teleconferences

eNewsletter: Myeloma Minute

IMF InfoLine: 1-800-452-CURE | 9am to 4pm PST

You are Not Alone

Questions?

Closing Comments

Kelly Cox and Dr. Joseph Mikhael

International Myeloma Foundation

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